STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 124713

TO: Shailendra Kumar **Location: 5d61 / 5c18** **Tuesday, June 22, 2004** **Art Unit: 1621** **Phone: 272-0640** **Serial Number: 10 / 046622**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

Jan Please

Access DB# 104913

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: S. Kumar Examiner #: 64594 Date: 6/15/04

Art Unit: 1621 Phone Number ~~30~~ 272-0610 Serial Number: 10/046,622

Mail Box and Bldg/Room Location: REM 5D61 Results Format Preferred (circle): PAPER DISK E-MAIL

5C18

If more than one search is submitted, please prioritize searches in order of need.

****

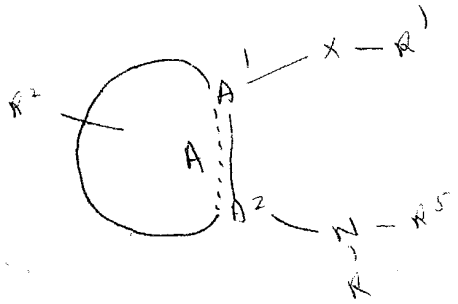
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Substituted amine derivatives and methods of use.

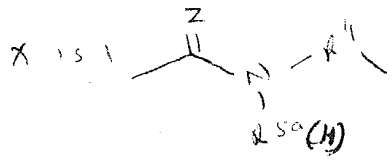
Inventors (please provide full names): Guoqing Chen et al

Earliest Priority Filing Date: 1/12/2001

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



A is six membered heteroaryl

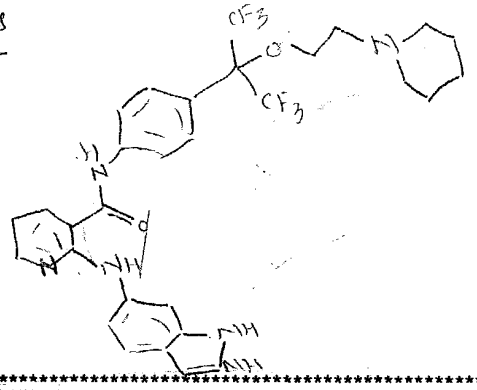


Z is O or S

R is substituted 4-6 membered heterocyclyl, aryl, bicyclic or tricyclic heterocyclyl.

R¹ is 6-10 membered aryl, 4-6 membered heterocyclyl cycloalkyl etc.

Species



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STAFF USE ONLY

Searcher: Jan

Searcher Phone #: 22504

Searcher Location:

Date Searcher Picked Up: 6/21

Date Completed: 6/22

Searcher Prep & Review Time:

Clerical Prep Time: 30

Online Time: 1+20

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#) 1

Bibliographic

Litigation

Fulltext

Patent Family

Other

Vendors and cost where applicable

STN ✓

Dialog

Questel/Orbit

Dr.Link

Lexis/Nexis

Sequence Systems

WWW/Internet

Other (specify) ✓

RECEIVED JUN 15 2004 TECH CENTER 1600/2900

PTO-1590 (8-01)

L Number	Hits	Search Text	DB	Time stamp
1	2200	(546/194,199).CCLS.	USPAT; US-PGPUB	2004/06/22 14:12
2	1249	(514/318).CCLS.	USPAT; US-PGPUB	2004/06/22 14:13

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STRUCTURE FILE UPDATES:   21 JUN 2004  HIGHEST RN 697224-75-2
DICTIONARY FILE UPDATES:  21 JUN 2004  HIGHEST RN 697224-75-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
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http://www.cas.org/ONLINE/DBSS/registryss.html

=> d l2 ide can

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   454481-33-5  REGISTRY
CN   3-Pyridinecarboxamide, 2-(1H-indazol-6-ylamino)-N-[4-[2,2,2-trifluoro-1-[2-
     (1-piperidinyl)ethoxy]-1-(trifluoromethyl)ethyl]phenyl]- (9CI)  (CA INDEX
     NAME)
FS   3D CONCORD
MF   C29 H28 F6 N6 O2
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); USES
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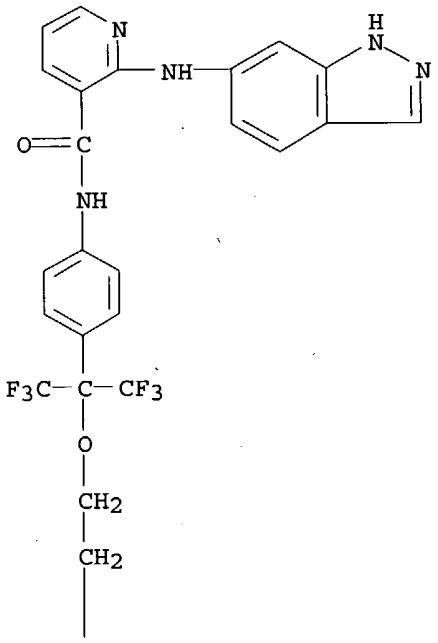

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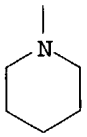

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:350636

REFERENCE 2: 137:216945

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DEL HIS

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L2 1 S L1 AND NC5/ES AND C6/ES AND N2C3-C6/ES
SEL RN
L3 0 S E1/CRN

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     FILE 'USPATFULL, USPAT2' ENTERED AT 07:25:50 ON 22 JUN 2004
L6              2 S L2

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 07:25:57 ON 22 JUN 2004
L7              3 DUP REM L5 L6 (1 DUPLICATE REMOVED)

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FILE 'HCAPLUS' ENTERED AT 07:26:18 ON 22 JUN 2004
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FILE 'USPATFULL' ENTERED AT 07:26:18 ON 22 JUN 2004
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FILE 'USPAT2' ENTERED AT 07:26:18 ON 22 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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L7   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN   2003:855655  HCAPLUS
DN   139:350636
TI   Preparation of amino heteroaryl amides for use in pharmaceutical
     compositions for the treatment of angiogenesis mediated diseases such as
     cancer
IN   Patel, Vinod F.; Askew, Benny; Booker, Shon; Chen, Guoqing; Dipietro,
     Lucian V.; Germain, Julie; Habgood, Gregory J.; Huang, Qi; Kim, Tae-seong;
     Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Riahi, Babak; Yuan, Chester
     Chenguang; Elbaum, Daniel
PA   Amgen Inc., USA
SO   U.S. Pat. Appl. Publ., 148 pp., Cont.-in-part of U.S. Ser. No. 46,622.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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     US 2003195230      A1    20031016       US 2002-46622    20020110
     WO 2004007481      A2    20040122       WO 2003-US22275  20030715
     WO 2004007481      A3    20040219
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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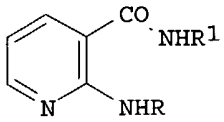

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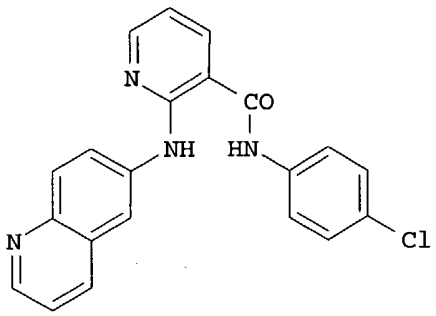


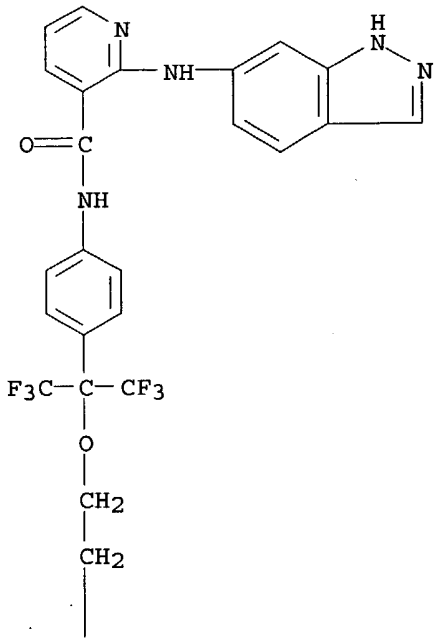
II

AB Amino substituted heteroaryl amides, such as I [R = nitrogen containing heteroaryl, such as quinolinyl, isoquinolinyl, indazolyl; R1 = aryl, cycloalkyl, heteroaryl, heterocyclyl], were prepared for therapeutic use. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compns. and methods for prophylaxis and treatment of cancer, angiogenesis related disorders, KDR-related disorders, cell proliferation related disorders, inflammation, reducing blood flow in tumors, reducing tumor size and diabetic retinopathy. Thus, amide II was prepared via an amination reaction of 2-chloronicotinic acid with 6-aminoquinoline followed by an amidation reaction of the aminonicotinic acid derivative thus formed with 4-chloroaniline. Biol. evaluations included HUVEC proliferation assay, inhibition of angiogenesis in the rat corneal neovascularization micropocket model, and antitumor activity using A431 rat tumor cells.

IT **454481-33-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of angiogenesis mediated diseases such as cancer)

RN 454481-33-5 HCAPLUS
CN 3-Pyridinecarboxamide, 2-(1H-indazol-6-ylamino)-N-[4-[2,2,2-trifluoro-1-[2-(1-piperidinyl)ethoxy]-1-(trifluoromethyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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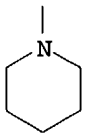

L7 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:676007 HCAPLUS
DN 137:216945
TI Preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases
IN Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Croghan, Michael; Dipietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Huang, Qi; Kim, Joseph L.; Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan, Chester Chenguang; Kim, Tae-Seong
PA Amgen Inc., USA
SO PCT Int. Appl., 395 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002068406	A2	20020906	WO 2002-US3064	20020111
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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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OS MARPAT 137:216945

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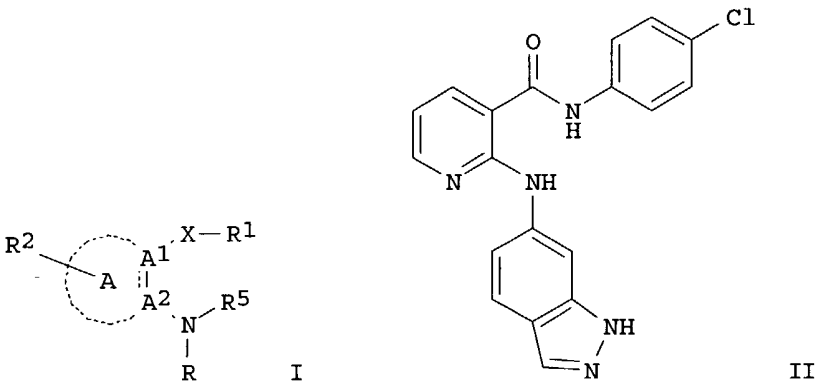


I II

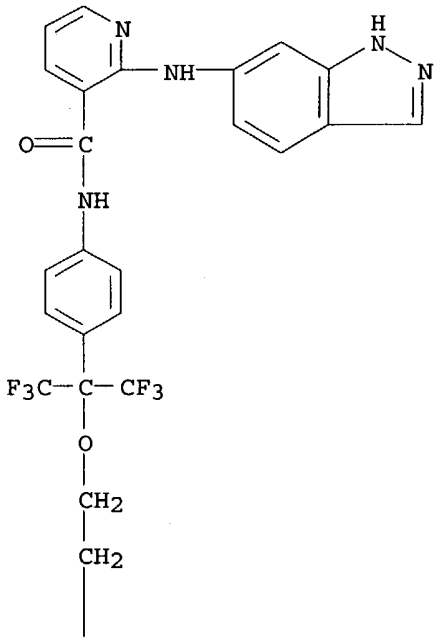
AB The title compds. [I; each of A1 and A2 = C, CH, N; A = 5-6 membered partially saturated heterocyclyl, 5-6 membered heteroaryl, 9-11 membered fused partially saturated heterocyclyl, etc.; X = C(:Z)N(R5a)R4; Z = O, S; R = (un)substituted 4-6 membered heterocyclyl, aryl, fused 9-14 membered bicyclic or tricyclic heterocyclyl; R1 = (un)substituted 6-10 membered aryl, 4-6 membered heterocyclyl, cycloalkyl, etc.; R2 = H, halo, cycloalkyl, etc.; R4 = a bond, alkylene, alkenylene, etc.; R5 = H, alkyl, (un)substituted Ph, aralkyl; R5a is not defined] which are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases, were prepared Thus, heating N-(4-chlorophenyl)-2-chloro-3-pyridinecarboxamide with 6-aminoindazole at 150° for 2 h afforded II which inhibited VEGF-stimulated HUVEC proliferation at level below 50 nM. Compds. I showed inhibition of KDR at doses less than 50 μM.

IT **454481-33-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

RN 454481-33-5 HCAPLUS

CN 3-Pyridinecarboxamide, 2-(1H-indazol-6-ylamino)-N-[4-[2,2,2-trifluoro-1-[2-(1-piperidinyl)ethoxy]-1-(trifluoromethyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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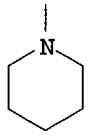

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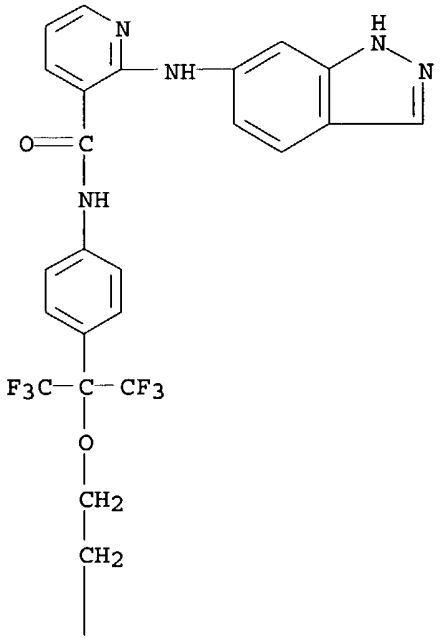
Adams, Jeffrey, Thousand Oaks, CA, UNITED STATES
Bemis, Jean, Arlington, MA, UNITED STATES
Pietro, Lucian Di, Gloucester, MA, UNITED STATES
Dominguez, Celia, Thousand Oaks, CA, UNITED STATES
Elbaum, Daniel, Newton, MA, UNITED STATES
Germain, Julie, Somerville, MA, UNITED STATES
Huang, Qi, Moorpark, CA, UNITED STATES
Kim, Joseph L., Wayland, MA, UNITED STATES
Ouyang, Xiaohu, Flushing, NY, UNITED STATES
Patel, Vinod F., Acton, MA, UNITED STATES
Smith, Leon M., Somerset, NJ, UNITED STATES
Tasker, Andrew, Simi Valley, CA, UNITED STATES
Xi, Ning, Thousand Oaks, CA, UNITED STATES
Xu, Shimin, Newbury Park, CA, UNITED STATES
Yuan, Chester Chenguang, Newbury Park, CA, UNITED STATES
Croghan, Michael, Ventura, CA, UNITED STATES
Kim, Tae-Seong, Thousand Oaks, CA, UNITED STATES
PI US 2003195230 A1 20031016
AI US 2002-46622 A1 20020110 (10)

PRAI US 2001-261882P 20010112 (60)
US 2001-323808P 20010919 (60)
DT Utility
FS APPLICATION
LREP AMGEN INCORPORATED, MAIL STOP 27-4-A, ONE AMGEN CENTER DRIVE, THOUSAND OAKS, CA, 91320-1799
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 9313
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Selected amines are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **454481-33-5P**
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)
RN 454481-33-5 USPATFULL
CN 3-Pyridinecarboxamide, 2-(1H-indazol-6-ylamino)-N-[4-[2,2,2-trifluoro-1-[2-(1-piperidinyl)ethoxy]-1-(trifluoromethyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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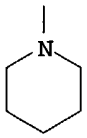


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DICTIONARY FILE UPDATES:  21 JUN 2004  HIGHEST RN 697224-75-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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  conducting SmartSELECT searches.

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=> d his

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L6              3 S L3 AND L4 NOT L5 SAM
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L8              5 S L3 AND L4 NOT L5 SAM SUB=L7

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                E E3+ALL
L11         11979 S E5+OLD,NT,PFT
                E E12+ALL
L12          2528 S E2+OLD,NT,PFT
                E E12+ALL
L13          4743 S E4+OLD,NT,PFT
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L15         25422 S L10-L14
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L30        2499 S L17  RAN=(2000:487683,2001:322939)

     FILE 'REGISTRY' ENTERED AT 09:13:46 ON 22 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 09:13:46 ON 22 JUN 2004
               SET SMARTSELECT ON
L31         SEL L30 1- RN :   40254 TERMS
               SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:14:42 ON 22 JUN 2004
L32       40254 S L31

     FILE 'HCAPLUS' ENTERED AT 09:17:25 ON 22 JUN 2004
               SET SMARTSELECT ON
L33         SEL L29 1- RN :   29322 TERMS
               SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:18:28 ON 22 JUN 2004
L34       29322 S L33

     FILE 'HCAPLUS' ENTERED AT 09:22:28 ON 22 JUN 2004
L35        2500 S L17  RAN=(2002:156220,)
L36        2500 S L17  RAN=(2001:322960,2002:155664)
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     FILE 'REGISTRY' ENTERED AT 09:23:20 ON 22 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 09:23:20 ON 22 JUN 2004
                SET SMARTSELECT ON
L37          SEL L35 1- RN :   52202 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:23:47 ON 22 JUN 2004
L38         52202 S L37

     FILE 'HCAPLUS' ENTERED AT 09:26:46 ON 22 JUN 2004
                SET SMARTSELECT ON
L39          SEL L36 1- RN :   45741 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:28:07 ON 22 JUN 2004
L40         45741 S L39

     FILE 'HCAPLUS' ENTERED AT 09:31:11 ON 22 JUN 2004
L41          1000 S L17  RAN=(2003:511283,)
L42           885 S L17  RAN=(2002:574858,2003:411091)
L43          1000 S L17  RAN=(2001:893846,2002:573393)
L44          1000 S L17  RAN=(2001:626282,2001:892462)
L45          1000 S L17  RAN=(2001:322960,2001:625451)
L46           115 S L18 NOT L41-L45

     FILE 'REGISTRY' ENTERED AT 09:34:23 ON 22 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 09:34:23 ON 22 JUN 2004
                SET SMARTSELECT ON
L47          SEL L41 1- RN :   52202 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:34:46 ON 22 JUN 2004
L48         52202 S L47

     FILE 'HCAPLUS' ENTERED AT 09:38:22 ON 22 JUN 2004
                SET SMARTSELECT ON
L49          SEL L42 1- RN :   53478 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:39:05 ON 22 JUN 2004
L50         53478 S L49

     FILE 'HCAPLUS' ENTERED AT 09:42:41 ON 22 JUN 2004
                SET SMARTSELECT ON
L51          SEL L43 1- RN :   37919 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:43:24 ON 22 JUN 2004
L52         37919 S L51

     FILE 'HCAPLUS' ENTERED AT 09:45:50 ON 22 JUN 2004
                SET SMARTSELECT ON
L53          SEL L44 1- RN :   20058 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:46:21 ON 22 JUN 2004
L54         20058 S L53

     FILE 'HCAPLUS' ENTERED AT 09:47:21 ON 22 JUN 2004
                SET SMARTSELECT ON
L55          SEL L45 1- RN :    8155 TERMS
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                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:47:48 ON 22 JUN 2004
L56         8155 S L55

     FILE 'HCAPLUS' ENTERED AT 09:48:14 ON 22 JUN 2004
                SET SMARTSELECT ON
L57          SEL L46 1- RN :   36539 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 09:48:35 ON 22 JUN 2004
L58        36539 S L57

     FILE 'HCAPLUS' ENTERED AT 09:51:20 ON 22 JUN 2004
L59          400 S L17  RAN=(2002:977961,2003:411091)
L60          485 S L17  RAN=(2002:574858,2002:977957)
L61          500 S L17  RAN=(2003:1007109,)
L62          500 S L41,L42 NOT L59-L61

     FILE 'REGISTRY' ENTERED AT 10:39:57 ON 22 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 10:39:58 ON 22 JUN 2004
                SET SMARTSELECT ON
L63          SEL L59 1- RN :   41934 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 10:40:34 ON 22 JUN 2004
L64        41934 S L63

     FILE 'HCAPLUS' ENTERED AT 10:43:49 ON 22 JUN 2004
                SET SMARTSELECT ON
L65          SEL L60 1- RN :   35868 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 10:44:22 ON 22 JUN 2004
L66        35868 S L65

     FILE 'HCAPLUS' ENTERED AT 10:46:44 ON 22 JUN 2004
                SET SMARTSELECT ON
L67          SEL L61 1- RN :   52202 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 10:47:12 ON 22 JUN 2004
L68        52202 S L67

     FILE 'HCAPLUS' ENTERED AT 10:50:04 ON 22 JUN 2004
                SET SMARTSELECT ON
L69          SEL L62 1- RN :   50577 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 10:50:43 ON 22 JUN 2004
L70        50577 S L69

     FILE 'HCAPLUS' ENTERED AT 10:54:30 ON 22 JUN 2004
L71         1000 S L61,L62
L72         1000 S L71 OR L71
L73          100 S L72  RAN=(2004:371055,)
L74          100 S L72  RAN=(2004:252604,2004:371053)
L75          100 S L72  RAN=(2004:142866,2004:252541)
L76          100 S L72  RAN=(2004:60240,2004:142807)
L77          100 S L72  RAN=(2003:1007109,2004:60205)
L78          100 S L72  RAN=(2003:913164,2003:1007021)
L79          100 S L72  RAN=(2003:818147,2003:913039)
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L80          100 S L72  RAN=(2003:719261,2003:818143)
L81          100 S L72  RAN=(2003:610468,2003:719252)
L82          100 S L72  RAN=(,2003:610454)

     FILE 'REGISTRY' ENTERED AT 11:07:16 ON 22 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 11:07:16 ON 22 JUN 2004
                SET SMARTSELECT ON
L83           SEL L73 1- RN :   30112 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:07:32 ON 22 JUN 2004
L84        30112 S L83

     FILE 'HCAPLUS' ENTERED AT 11:10:12 ON 22 JUN 2004
                SET SMARTSELECT ON
L85           SEL L74 1- RN :   30109 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:10:27 ON 22 JUN 2004
L86        30109 S L85

     FILE 'HCAPLUS' ENTERED AT 11:12:09 ON 22 JUN 2004
                SET SMARTSELECT ON
L87           SEL L75 1- RN :   12509 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:12:19 ON 22 JUN 2004
L88        12509 S L87

     FILE 'HCAPLUS' ENTERED AT 11:14:06 ON 22 JUN 2004
                SET SMARTSELECT ON
L89           SEL L76 1- RN :   11572 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:14:15 ON 22 JUN 2004
L90        11572 S L89

     FILE 'HCAPLUS' ENTERED AT 11:14:57 ON 22 JUN 2004
                SET SMARTSELECT ON
L91           SEL L78 1- RN :   18549 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:15:09 ON 22 JUN 2004
L92        18549 S L91

     FILE 'HCAPLUS' ENTERED AT 11:16:19 ON 22 JUN 2004
                SET SMARTSELECT ON
L93           SEL L79 1- RN :    8264 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:16:25 ON 22 JUN 2004
L94         8264 S L93

     FILE 'HCAPLUS' ENTERED AT 11:16:53 ON 22 JUN 2004
                SET SMARTSELECT ON
L95           SEL L80 1- RN :    9088 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:17:00 ON 22 JUN 2004
L96         9088 S L95

     FILE 'HCAPLUS' ENTERED AT 11:17:30 ON 22 JUN 2004
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```
                SET SMARTSELECT ON
L97          SEL L81 1- RN :   11056 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:17:38 ON 22 JUN 2004
L98         11056 S L97
L99        364795 S L24,L26,L28,L32,L34,L38,L40,L48,L50,L52,L54,L56,L58,L64,L66,L
L100            4 S L3 SAM SUB=L99
L101          212 S L3 FUL SUB=L99
                SAV L101 KUMAR046/A

     FILE 'HCAPLUS' ENTERED AT 11:22:34 ON 22 JUN 2004
L102           68 S L101
L103           31 S L102 AND (PD<=20010112 OR PRD<=20010112 OR AD<=20010112)
L104            8 S L103 AND L15,L21
                E AMGEN/PA,CS
L105            5 S L103 AND AMGEN?/PA,CS
L106            5 S L103 AND (CHEN G? OR ADAMS J? OR BEMIS J? OR DIPIETRO L? OR D
L107            2 S L103 AND L9
L108            8 S L104-L107
L109           61 S L101 (L) (THU OR DMA OR PAC OR PKT)/RL
L110           65 S L101 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
L111           30 S L103 AND L109,L110
L112           22 S L111 NOT L108

     FILE 'REGISTRY' ENTERED AT 11:27:21 ON 22 JUN 2004

=> d l3
L3 HAS NO ANSWERS
L3                STR
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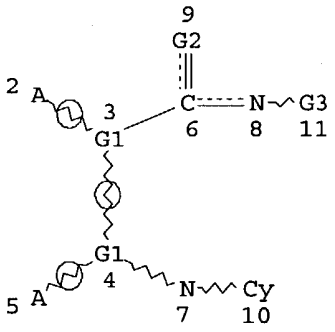

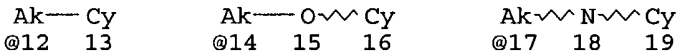

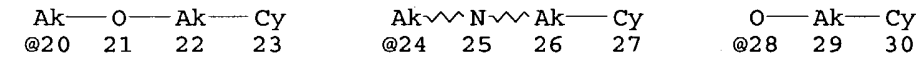

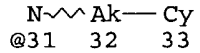


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VAR G1=C/N
VAR G2=O/S
VAR G3=CY/12/14/17/20/24/28/31
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  32
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STEREO ATTRIBUTES: NONE

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:27:34 ON 22 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 22 Jun 2004 VOL 140 ISS 26
FILE LAST UPDATED: 21 Jun 2004 (20040621/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d all fhitstr tot l108

L108 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:950057 HCAPLUS
DN 140:16647
ED Entered STN: 05 Dec 2003
TI Preparation of 2-aminopyridine-3-carboxamides as remedies for **angiogenesis** mediated diseases
IN Askew, Benny; **Adams, Jeffrey**; Booker, Shon; **Chen, Guoqing**; **Dipietro, Lucian V.**; **Elbaum, Daniel**; **Germain, Julie**; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Handley, Michael; **Huang, Qi**; **Kim, Tae-seong**; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; **Patel, Vinod F.**; Riahi, Babak; **Kim, Joseph L.**; **Xi, Ning**; Yang, Kevin; **Yuan, Chester Chenguang**
PA **Amgen Inc., USA**
SO U.S. Pat. Appl. Publ., 252 pp., Cont.-in-part of U.S. Ser. No. 46,681.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-506
ICS A61K031-4745; A61K031-444; A61K031-4439; C07D471-02; C07D403-02; C07D405-02; C07D413-02
NCL 514256000; 514303000; 514314000; 514332000; 514337000; 514336000; 544333000; 546176000; 546113000; 546262000
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003225106	A1	20031204	US 2002-197974	20020717 <--
US 2003125339	A1	20030703	US 2002-46681	20020110 <--
WO 2004007458	A1	20040122	WO 2003-US22417	20030715

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

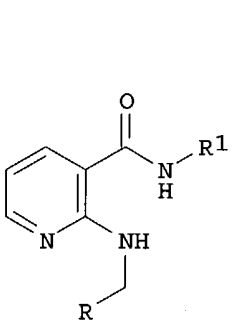
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-261339P P 20010112 <--
US 2001-323764P P 20010919
US 2002-46681 A2 20020110
US 2002-197974 A 20020717

OS MARPAT 140:16647

GI



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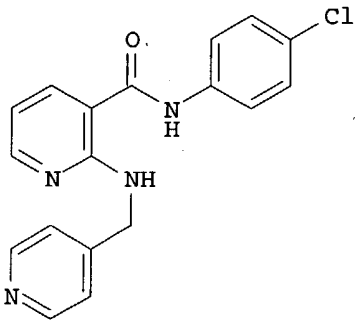

II

AB The title compds. [I; R = (un)substituted 4-pyridyl, 2-pyridyl, 4-pyrimidinyl, 4-quinolyl, etc.; R1 = (un)substituted aryl, cycloalkyl, 5-6 membered heteroaryl, 9-10 membered bicyclic and 11-14 membered tricyclic heterocyclyl], which are effective for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like, were prepared Thus, the title compound II was prepared from 2-aminonicotinic acid, 4-chloroaniline, and 4-pyridinecarboxaldehyde. The compds. I showed inhibition of KDR kinase at < 50 μM. Many compds. I inhibited VEGF-stimulated HUVEC proliferation at a level below 50 nM. Pharmaceutical composition comprising the compound I is claimed.

ST aminopyridinecarboxamide prepn antitumor VEGFR KDR kinase inhibitor; pyridinecarboxamide prepn **angiogenesis** mediated disease VEGFR KDR kinase inhibitor

IT Cytotoxic agents
(antimetabolites, co-administration; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration with interferon-type agents; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT Alkylating agents, biological
Antibiotics
Immunomodulators
(co-administration; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration; preparation of 2-aminopyridine-3-carboxamides for

treating **angiogenesis** mediated diseases)

IT Eye, disease
(diabetic retinopathy, treatment of; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT **Angiogenesis**
(**neovascularization**, **eye**, treatment of corneal **neovascularization**; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT **Eye, disease**
(**neovascularization**, treatment of corneal **neovascularization**; preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT **Angiogenesis**
Angiogenesis inhibitors
Anti-inflammatory agents
Antitumor agents
Cell proliferation
Human
Inflammation
Neoplasm
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 150977-45-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 453561-03-0P 453561-73-4P 453561-77-8P 453561-95-0P 453562-69-1P
453562-83-9P 453563-07-0P 453563-37-6P 453563-79-6P 453564-01-7P
629651-31-6P 629651-56-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 352227-57-7P, 2-[(Pyridin-4-ylmethyl)amino]-N-(3-trifluoromethylphenyl)nicotinamide 352227-65-7P 352227-72-6P
352227-74-8P 453560-98-0P 453561-00-7P 453561-01-8P 453561-02-9P
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453561-35-8P 453561-36-9P 453561-37-0P 453561-38-1P 453561-39-2P
453561-40-5P 453561-41-6P 453561-42-7P 453561-43-8P 453561-44-9P
453561-45-0P 453561-46-1P 453561-47-2P 453561-48-3P 453561-49-4P
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453561-67-6P 453561-68-7P 453561-69-8P 453561-70-1P 453561-71-2P
453561-72-3P 453561-75-6P 453561-76-7P 453561-78-9P 453561-80-3P
453561-81-4P, 2-[(2,3-Dihydrobenzofuran-5-ylmethyl)amino]-N-[3,3-dimethyl-1-(piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]nicotinamide
453561-82-5P 453561-83-6P 453561-84-7P 453561-85-8P,
N-[1-(2-Aminoacetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxypyridin-4-ylmethyl)amino]nicotinamide 453561-86-9P,
N-[1-(2-Aminoacetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-87-0P, (S)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-88-1P, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-89-2P, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-90-5P, (S)-N-[3-(Pyrrolidin-2-

ylmethoxy)-5-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-92-7P, N-[3-(Piperidin-4-yloxy)-5-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-93-8P, N-[4-tert-Butyl-3-[(piperidin-4-yl)methoxy]phenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-94-9P, N-[4-tert-Butyl-3-(pyrrolidin-2-ylmethoxy)phenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-96-1P 453561-97-2P 453561-98-3P
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453562-62-4P 453562-65-7P 453562-66-8P 453562-75-9P 453562-76-0P
453562-80-6P 453562-81-7P 453562-84-0P 453562-85-1P 453562-86-2P
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453563-42-3P 453563-43-4P 453563-44-5P 453563-45-6P 453563-46-7P
453563-47-8P 453563-48-9P 453563-49-0P 453563-50-3P 453563-51-4P
453563-52-5P 453563-53-6P 453563-54-7P 453563-55-8P 453563-56-9P
453563-57-0P 453563-58-1P 453563-59-2P 453563-60-5P 453563-61-6P
453563-62-7P 453563-63-8P 453563-64-9P 453563-65-0P 453563-66-1P
453563-67-2P 453563-68-3P 453563-69-4P 453563-70-7P 453563-71-8P
453563-72-9P 453563-73-0P 453563-74-1P 453563-75-2P 453563-76-3P
453563-77-4P 453563-78-5P 453563-80-9P 453563-81-0P 453563-82-1P
453563-83-2P 453563-84-3P 453563-85-4P 453563-86-5P 453563-87-6P
453563-88-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 453563-89-8P 453563-90-1P 453563-91-2P 453563-92-3P 453563-93-4P
453563-94-5P 453563-95-6P 453563-96-7P 453563-97-8P 453563-98-9P
453563-99-0P 453564-00-6P 453564-02-8P 453564-03-9P 453564-04-0P
453564-05-1P 453564-06-2P 453564-07-3P 453564-08-4P 453564-09-5P
453564-10-8P 453564-11-9P 453564-12-0P 453564-13-1P 453564-14-2P
453564-15-3P **453564-16-4P** 453564-17-5P 453564-18-6P
453564-19-7P 453564-20-0P 453564-21-1P 453564-22-2P 453564-23-3P
453564-24-4P 453564-25-5P 453564-26-6P 453564-27-7P 453564-28-8P
453564-30-2P 453564-31-3P 453564-32-4P 453564-33-5P 453564-34-6P
453564-36-8P 453564-37-9P 453564-38-0P 453564-39-1P 453564-40-4P
453564-41-5P 453564-42-6P 453564-43-7P 453564-44-8P 453564-45-9P
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453565-16-7P 453565-17-8P 453565-18-9P 453565-19-0P 453565-20-3P
453565-21-4P 453565-22-5P 453565-23-6P 453565-24-7P 453565-25-8P
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629651-16-7P 629651-17-8P 629651-18-9P 629651-19-0P 629651-20-3P
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629651-32-7P 629651-33-8P 629651-34-9P 629651-35-0P 629651-36-1P
629651-37-2P 629651-38-3P 629651-39-4P **629651-40-7P**
629651-41-8P 629651-42-9P 629651-43-0P 629651-44-1P 629651-45-2P
629651-46-3P 629651-47-4P 629651-48-5P 629651-49-6P 629651-50-9P
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629651-68-9P 629651-69-0P 629651-70-3P 629651-71-4P 629651-72-5P
629651-73-6P 629651-74-7P 629651-75-8P 629651-76-9P 629651-77-0P
629651-78-1P 629651-79-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 629651-80-5P 629651-81-6P 629651-82-7P 629651-83-8P 629651-84-9P
629651-85-0P 629651-86-1P 629651-87-2P 629651-88-3P 629651-89-4P
629651-90-7P 629651-91-8P 629651-92-9P 629651-93-0P 629651-94-1P
629651-98-5P 629651-99-6P 629652-00-2P 629652-01-3P 629652-02-4P
629652-03-5P 629656-02-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 55-86-7 79-04-9, Chloroacetyl chloride 98-16-8, 3-(Trifluoromethyl)aniline 99-09-2, 3-Nitroaniline 99-57-0, 2-Amino-4-nitrophenol 99-88-7, 4-Isopropylaniline 106-47-8, 4-Chloroaniline, reactions 106-52-5, 4-Hydroxy-1-methylpiperidine 108-01-0, N,N-Dimethylethanolamine 108-23-6, Isopropyl chloroformate 109-01-3, N-Methylpiperazine 109-72-8, Butyllithium, reactions 110-89-4, Piperidine, reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride 123-00-2, 4-Morpholinepropanamine 139-59-3, 4-Phenoxyaniline 288-88-0, 1H-1,2,4-Triazole 328-79-0, 1-Methoxy-3-nitro-5-trifluoromethylbenzene 328-80-3 350-46-9, 1-Fluoro-4-nitrobenzene 372-48-5, 2-Fluoropyridine 527-72-0, 2-Thienylcarboxylic acid 541-41-3, Ethyl chloroformate 609-71-2, 2-Hydroxynicotinic acid 628-13-7, Pyridine hydrochloride 722-92-9, 2-(4-Aminophenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol 769-92-6, 4-tert-Butylaniline 872-85-5, 4-Pyridinecarboxaldehyde 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1118-68-9, Dimethylaminoacetic acid 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 1445-73-4, N-Methyl-4-piperidone 1458-98-6, 3-Bromo-2-methylpropene 1692-15-5, 4-Pyridylboronic acid 1704-62-7, 2-[2-(Dimethylamino)ethoxy]ethanol 2008-75-5, 1-(2-Chloroethyl)piperidine hydrochloride 2221-00-3, (4-Imidazolylphenyl)amine 2435-50-9, Pyrimidine-4-carboxaldehyde

2942-59-8, 2-Chloronicotinic acid 3040-44-6, 2-(Piperid-1-yl)ethanol 3279-07-0, 2-Nitro-4-tert-butylphenol 3282-56-2, 4-tert-Butylnitrobenzene 3438-46-8, 4-Methylpyrimidine 3554-65-2 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 3731-53-1, 4-Aminomethylpyridine 4009-98-7, Methoxymethyltriphenylphosphonium chloride 4160-54-7, 1,3-Dinitro-4-tert-butylbenzene 4769-96-4, 6-Nitroindole 5345-47-1, 2-Aminonicotinic acid 5458-84-4, 2-Iodo-5-nitroanisole 5909-24-0, Ethyl 4-chloro-2-methylthiopyrimidine-5-carboxylate 6146-52-7, 5-Nitroindole 6165-69-1, 3-Thiopheneboronic acid 6310-21-0, 2-tert-Butylaniline 6457-49-4, 4-Piperidylmethanol 7216-42-4 7223-38-3, 1-Dimethylamino-2-propyne 10403-47-1, 2-Bromo-5-nitroaniline 13258-63-4, 4-(2-Aminoethyl)pyridine 14446-67-4, 1-Allylpiperidine 19727-83-4, 6-Nitroindoline 19910-33-9, 2-(4-Nitrophenyl)propionic acid 20769-85-1, 2-Bromo-2-methylpropionyl bromide 22288-78-4, Methyl 3-amino-2-thiophenecarboxylate 24424-99-5, Di-tert-butyl dicarbonate 24954-67-4, 2-(4-Nitrophenyl)ethylamine 30529-70-5, 2-Chloro-6-methylnicotinic acid 33252-30-1, 2-Chloro-4-cyanopyridine 51149-08-7 54962-75-3, 3-Bromo-5-(trifluoromethyl)phenylamine 57260-71-6, N-Boc-piperazine 60979-14-8, 1-Nitro-4-(1,1,2,2,2-pentafluoroethyl)benzene 69610-40-8 71999-74-1 74764-17-3, 2-(2-Pyridylamino)ethylamine 75833-38-4, 2-Chloropyrimidine-4-carbonitrile 80887-01-0, 2-Bromo-5-nitrobenzoyl chloride 102362-98-1, 3,3-Dimethyl-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 105612-50-8 109384-19-2, 1-Boc-4-hydroxypiperidine 110073-17-1, Methyl 2-(morpholin-4-yl)propionate 119899-26-2, 2-Fluoropyridine-3-carbonyl chloride 148546-99-0, 3-(4-Methylpiperazinyl)phenylamine 171178-50-0, 2,6-Difluoropyridine-3-carboxylic acid 183946-06-7, 2-Methyl-4-nitro-1-pentafluoroethylbenzene 201733-56-4 453560-55-9, 1-Boc-2-(3-nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-61-7, 3,3-Dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-6-nitro-2,3-dihydro-1H-indole 453560-62-8 453560-64-0, 2-Methoxy-4-nitro-1-pentafluoroethylbenzene 453560-68-4 453560-72-0, (S)-2-Chloro-N-[4-(2-oxiranylmethoxy)-3-pentafluoroethylphenyl]nicotinamide 453560-93-5, 1-Methyl-4-[1-methyl-1-(4-nitrophenyl)ethyl]pyridinium 453561-19-8 453561-74-5 453563-30-9, 2-Fluoro-N-(4-trifluoromethylphenyl)nicotinamide 453563-31-0, [[2-(1-Isopropylazetidin-3-ylmethoxy)pyridin-4-yl]methyl]amine 453564-35-7, 2-Amino-N-(4-pentafluoroethylphenyl)nicotinamide 618446-18-7 618446-37-0 618446-39-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT 349-57-5P, 3-Nitro-5-trifluoromethylphenol 393-55-5P, 2-Fluoronicotinic acid 6310-17-4P, 2-Bromo-1-tert-butyl-4-nitrobenzene 6425-46-3P, 4-[(4-Nitrophenyl)methyl]morpholine 13669-28-8P, 1-Methyl-4-methylenepiperidine 16153-81-4P, 4-Methyl-1-(4-aminophenyl)piperazine 16155-03-6P, 4-Methyl-1-(4-nitrophenyl)piperazine 18755-53-8P, 2-Methyl-2-(4-nitrophenyl)propan-1-ol 20691-89-8P, (1-Methylpiperidin-4-yl)methanol 24252-37-7P, 1-Methylpiperidine-4-carboxylic acid ethyl ester 29241-65-4P, 5-Bromo-2-chloronicotinic acid 51013-67-3P, 4-(Morpholin-4-ylmethyl)phenylamine 51444-31-6P, 2-(1,2,4-Triazolyl)ethylamine 53062-99-0P 54815-23-5P, 2-(4-Aminophenyl)-2-methylpropionic acid methyl ester 56329-05-6P 57841-51-7P 59115-08-1P, 2-Methyl-2-(4-nitrophenyl)propionic acid methyl ester 60979-04-6P, 4-(1,1,2,2,2-Pentafluoroethyl)phenylamine 69296-06-6P, 2-Morpholin-4-ylpropanol 72716-86-0P, 4-Cyano-2-methoxypyridine 85160-84-5P, 2,2-Dimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 90221-50-4P, N-(2-Bromo-5-nitrophenyl)acetamide 91133-58-3P 94838-59-2P 100973-67-9P 101537-64-8P, 3-[(tert-Butoxy)carbonylamino]thiophene-2-carboxylic acid 103392-84-3P, 2-tert-Butyl-5-nitroaniline 103394-70-3P, 4-tert-Butyl-3-nitrophenylamine 104612-36-4P, 5-Bromo-2-hydroxynicotinic acid 105807-77-0P, 2,2,4-Trimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 105807-84-9P, 6-Amino-2,2-dimethyl-4H-

benzo[1,4]oxazin-3-one 106516-27-2P, 3-(1-Methyl-1,2,3,6-tetrahydropyridin-4-yl)-5-nitro-1H-indole 117242-06-5P, 4,4-Dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 136545-11-4P, 2,2-Dimethyl-6-nitro-3,4-dihydro-2H-benzo[1,4]oxazine 137076-22-3P, 1-Boc-4-formylpiperidine 140837-70-3P, 3,3-Dimethyl-6-nitro-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 142253-56-3P, 1-Boc-3-Hydroxymethylazetidine 142253-57-4P, Methanesulfonic acid N-Boc-azetidin-3-ylmethyl ester 142851-03-4P, 1-Boc-piperidine-4-carboxylic acid ethyl ester 143094-45-5P, 5-Bromo-2-chloro-N-(4-chlorophenyl)nicotinamide 144226-16-4P 144293-82-3P, 1-(2,2-Dimethyl-6-nitro-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 144293-83-4P, 1-(6-Amino-2,2-dimethyl-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 148900-69-0P, ((2-Methoxy-4-pyridyl)methyl)amine 149532-90-1P, ((2-Methoxypyridin-4-yl)methyl)amine hydrochloride 161975-39-9P, 1-Boc-4-methylsulfonyloxymethylpiperidine 179898-72-7P, 3,3-Dimethyl-6-nitroindoline 180692-27-7P, Trifluoromethanesulfonic acid 1-methyl-1,2,3,6-tetrahydropyridin-4-yl ester 181363-19-9P 182564-38-1P, 3-(1-Methyl-4-piperidyl)indole-5-ylamine 436095-35-1P, 3-[(4-Methylpiperazinyl)sulfonyl]phenylamine 442846-54-0P, [(2-(1-Methylpiperidin-4-yloxy)pyridin-4-yl)methyl]amine 442846-55-1P, [(2-(1-Methylpyrrolidin-2-ylmethoxy)pyridin-4-yl)methyl]amine 442846-56-2P, (4-Aminomethylpyridin-2-yl)(3-morpholin-4-ylpropyl)amine 442846-58-4P, [(2-(1-Methylpiperidin-4-ylmethoxy)pyridin-4-yl)methyl]amine 442846-59-5P, 3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethylphenylamine 442846-60-8P, (3-(4-Methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenyl)amine 442846-61-9P, 7-Amino-2-(4-methoxybenzyl)-4,4-dimethyl-3,4-dihydro-2H-isoquinolin-1-one 442846-62-0P, (3-Amino-5-trifluoromethylphenyl)(4-Boc-piperazin-1-yl)methanone 442846-63-1P, 1-(7-Amino-4,4-dimethyl-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-64-2P, 4-tert-Butyl-3-(1-Boc-pyrrolidin-3-ylmethoxy)phenylamine 442846-65-3P, 4-tert-Butyl-3-(1-Boc-azetidin-3-ylmethoxy)phenylamine 442846-67-5P, N-(4-Acetyl-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-68-6P, 2-Fluoro-N-(2,2,4-trimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)nicotinamide 442846-69-7P, N-(2,2-Dimethyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-70-0P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-71-1P, 2-Fluoro-N-(2-Boc-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-72-2P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenyl]nicotinamide 442846-73-3P, 2-Fluoro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-74-4P, 2-Fluoro-N-[3-((4-Boc-piperazin-1-yl)carbonyl)-5-trifluoromethylphenyl]nicotinamide 442846-75-5P, 2-Fluoro-N-[3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-76-6P, N-(2-Acetyl-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-fluoronicotinamide 442846-77-7P, N-[3,3-Dimethyl-1-(1-methylpiperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-fluoronicotinamide 442846-78-8P, 2-Fluoro-N-[3-(1-Boc-azetidin-3-ylmethoxy)-5-trifluoromethylphenyl]nicotinamide 442846-79-9P, (S)-N-[4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)phenyl]-2-fluoronicotinamide 442846-80-2P, 2-Chloro-N-[2-(4-methoxybenzyl)-4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl]nicotinamide 442846-81-3P, 2-Chloro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-82-4P, 2-[3-[(2-Chloropyridine-3-carbonyl)amino]phenyl]-2-methylpropionic acid methyl ester 442846-83-5P, N-[4-tert-Butyl-3-[2-(1-Boc-piperidin-4-yl)ethyl]phenyl]-2-chloronicotinamide 442846-84-6P 442846-85-7P 442846-86-8P 442846-87-9P 442846-88-0P, 1-[2-(2-tert-Butyl-5-nitrophenoxy)ethyl]piperidine 442846-90-4P 442846-91-5P, 1-(4,4-Dimethyl-7-nitro-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-92-6P, 2-Bromo-N-(4-methoxybenzyl)-5-nitrobenzamide 442846-93-7P, 4,4-Dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 442846-94-8P,

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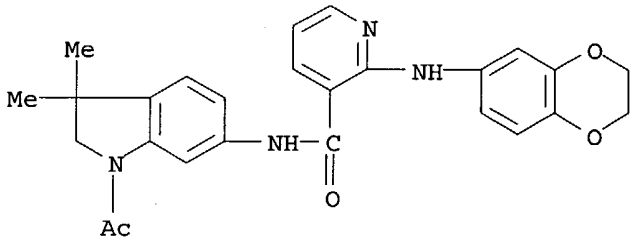
carboxamide 453563-09-2P, N-(4-tert-Butylphenyl)-2,6-difluoronicotinamide 453563-19-4P 629651-95-2P 629651-96-3P 629651-97-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

IT **453564-16-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating **angiogenesis** mediated diseases)

RN 453564-16-4 HCAPLUS
CN 3-Pyridinecarboxamide, N-(1-acetyl-2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(2,3-dihydro-1,4-benzodioxin-6-yl)amino]- (9CI) (CA INDEX NAME)



L108 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:855655 HCAPLUS
DN 139:350636
ED Entered STN: 31 Oct 2003
TI Preparation of amino heteroaryl amides for use in pharmaceutical compositions for the treatment of **angiogenesis** mediated diseases such as cancer
IN **Patel, Vinod F.**; Askew, Benny; Booker, Shon; **Chen, Guoqing**; **Dipietro, Lucian V.**; **Germain, Julie**; Habgood, Gregory J.; **Huang, Qi**; **Kim, Tae-seong**; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Riahi, Babak; **Yuan, Chester Chenguang**; **Elbaum, Daniel**
PA **Amgen Inc., USA**
SO U.S. Pat. Appl. Publ., 148 pp., Cont.-in-part of U.S. Ser. No. 46,622.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07D043-02
ICS C07D041-02; A61K031-517; A61K031-4439
NCL 514266210; 514338000; 544284000; 546273400; 546277100; 546275700
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 31, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003203922	A1	20031030	US 2002-197918	20020717 <--
	US 2003195230	A1	20031016	US 2002-46622	20020110 <--
	WO 2004007481	A2	20040122	WO 2003-US22275	20030715
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PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
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CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
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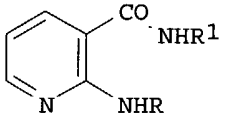
PRAI US 2001-261882P P 20010112 <--
US 2001-323808P P 20010919 <--
US 2002-46622 A2 20020110
US 2002-197918 A 20020717

OS MARPAT 139:350636

GI



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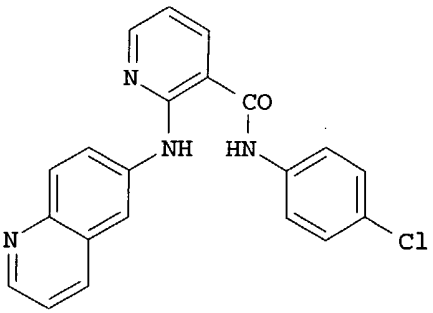

II

AB Amino substituted heteroaryl amides, such as I [R = nitrogen containing heteroaryl, such as quinolinyl, isoquinolinyl, indazolyl; R1 = aryl, cycloalkyl, heteroaryl, heterocyclyl], were prepared for therapeutic use. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compns. and methods for prophylaxis and treatment of cancer, **angiogenesis** related disorders, KDR-related disorders, cell proliferation related disorders, inflammation, reducing blood flow in tumors, reducing tumor size and diabetic retinopathy. Thus, amide II was prepared via an amination reaction of 2-chloronicotinic acid with 6-aminoquinoline followed by an amidation reaction of the aminonicotinic acid derivative thus formed with 4-chloroaniline. Biol. evaluations included HUVEC proliferation assay, inhibition of **angiogenesis** in the rat corneal **neovascularization** micropocket model, and antitumor activity using A431 rat tumor cells.

ST heteroaryl amide prepn **angiogenesis** inhibitor; KDR related disorder treatment heteroaryl amide prepn; proliferation related disorder treatment heteroaryl amide prepn; inflammation treatment heteroaryl amide prepn; diabetic retinopathy treatment heteroaryl amide prepn; cancer tumor treatment heteroaryl amide prepn; antitumor agents heteroaryl amide prepn; antiinflammatory agent heteroaryl amide prepn

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KDR, disorders; preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT Eye, disease
(diabetic retinopathy, treatment; preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT **Angiogenesis inhibitors**
Anti-inflammatory agents

Antitumor agents
Cytotoxic agents
Human
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT Drug delivery systems
(prodrugs; preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT Inflammation
Neoplasm
(treatment; preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT **454480-74-1P 454481-03-9P 454481-08-4P**
454481-54-0P 454481-69-7P 454481-80-2P
454481-81-3P 454481-82-4P 618445-79-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT **453564-50-6P 454480-67-2P 454480-68-3P**
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454480-79-6P 454480-80-9P 454480-81-0P
454480-82-1P 454480-83-2P 454480-84-3P
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618445-28-6P 618445-29-7P 618445-30-0P
618445-31-1P 618445-32-2P 618445-33-3P

618445-34-4P 618445-35-5P 618445-36-6P
618445-37-7P 618445-38-8P 618445-39-9P
618445-40-2P 618445-41-3P 618445-42-4P
618445-43-5P 618445-44-6P 618445-45-7P
618445-46-8P 618445-47-9P 618445-48-0P
618445-49-1P 618445-50-4P 618445-51-5P
618445-52-6P 618445-53-7P 618445-54-8P
618445-55-9P 618445-56-0P 618445-57-1P
618445-58-2P 618445-59-3P 618445-60-6P
618445-61-7P 618445-62-8P 618445-63-9P
618445-64-0P 618445-65-1P 618445-66-2P
618445-67-3P 618445-68-4P 618445-69-5P
618445-70-8P 618445-71-9P 618445-72-0P
618445-73-1P 618445-74-2P 618445-75-3P
618445-76-4P 618445-77-5P 618445-78-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT 51-75-2, Bis(2-chloroethyl)methylamine 55-86-7, Methyl-bis-(2-chloroethyl)amine hydrochloride 70-34-8, 2,4-Dinitrofluorobenzene 75-03-6, Iodoethane 75-89-8, 2,2,2-Trifluoroethanol 99-57-0, 2-Amino-4-nitrophenol 99-88-7, 4-Isopropylaniline 102-28-3, 3'-Aminoacetanilide 105-67-9, 2,4-Dimethylphenol 106-47-8, 4-Chloroaniline, reactions 106-52-5, 4-Hydroxy-N-methylpiperidine 108-01-0, N,N-Dimethylethanolamine 109-01-3, N-Methylpiperazine 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 111-77-3, 2-(2-Methoxyethoxy)ethan-1-ol 123-00-2, 4-(3-Aminopropyl)morpholine 123-75-1, Pyrrolidine, reactions 139-59-3, 4-Phenoxyaniline 271-63-6, 1H-Pyrrolo[2,3-b]pyridine 328-79-0, 1-Methoxy-3-nitro-5-trifluoromethylbenzene 328-80-3 360-54-3, Methyl 2-(trifluoromethyl)-3,3,3-trifluoropropionate 372-47-4, 3-Fluoropyridine 372-48-5, 2-Fluoropyridine 401-99-0, 3,5-Dinitrobenzotrifluoride 536-33-4 555-21-5, 4-Nitrophenylacetonitrile 555-68-0, 3-Nitrocinnamic acid 580-15-4, 6-Aminoquinoline 598-21-0, Bromoacetyl bromide 619-17-0, 2-Amino-4-nitrobenzoic acid 624-28-2, 2,5-Dibromopyridine 643-43-6, (2,4-Dinitrophenyl)acetic acid 722-92-9, 4-[2,2,2-Trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenylamine 769-92-6, 4-tert-Butylaniline 814-68-6, Acryloyl chloride 1068-57-1, Acetic acid hydrazide 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1118-68-9, Dimethylaminoacetic acid 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 1202-00-2, [2-(2-Aminophenoxy)ethyl]dimethylamine 1445-73-4, 1-Methyl-4-piperidone 1458-98-6, 3-Bromo-2-methylpropene 1692-15-5, 4-Pyridylboronic acid 2008-75-5, 1-(2-Chloroethyl)piperidine monohydrochloride 2314-97-8, Trifluoromethyl iodide 2393-23-9, 4-Methoxybenzylamine 2402-67-7 2942-59-8, 2-Chloronicotinic acid 3240-94-6, 4-(2-Chloroethyl)morpholine 3279-07-0, 2-Nitro-4-tert-butylphenol 3282-56-2, 1-(tert-Butyl)-4-nitrobenzene 3350-78-5, 3,3-Dimethylacryloyl chloride 3389-21-7, 3-(2-Bromoethyl)-1H-indole 3438-46-8, 4-Methylpyrimidine 3731-53-1, Pyridin-4-ylmethylamine 4009-98-7, Methoxymethyltriphenylphosphonium chloride 4160-54-7, 1,3-Dinitro-4-tert-butylbenzene 4637-24-5, Dimethylformamide dimethyl acetal 4769-96-4, 6-Nitroindole 4920-79-0, 2-Chloro-4-nitroanisole 5332-96-7, 1-(4-Nitrophenyl)propan-2-one 5458-84-4, 2-Iodo-5-nitroanisole 5600-21-5, 2-Amino-4-chloro-6-methylpyrimidine 6146-52-7, 5-Nitroindole 6310-21-0, 2-tert-Butylaniline 6313-33-3, Formamidine monohydrochloride 6967-12-0, 6-Aminoindazole 7223-38-3, 1-Dimethylamino-2-propyne 7364-33-2 7597-18-4, 6-Nitroindazole 10403-47-1, 2-Bromo-5-nitroaniline 14446-67-4, 1-Allylpiperidine 19727-83-4, 6-Nitroindoline 19798-81-3, 2-Amino-6-bromopyridine 19910-33-9, 2-(4-Nitrophenyl)propionic acid 20769-85-1, 2-Bromo-2-methylpropionyl bromide 22245-96-1 33252-30-1,

2-Chloro-4-cyanopyridine 33786-89-9, 5-Chlorobenzene-1,3-diamine 49609-84-9, 2-Chloronicotinoyl chloride 49844-90-8, 4-Chloro-2-methylsulfanylpyrimidine 51149-08-7, 3,6-Dichloropyridazine-4-carboxylic acid 51304-58-6 53062-99-0 54962-75-3, 3-Bromo-5-(trifluoromethyl)phenylamine 57260-71-6, N-Boc-piperazine 59382-59-1, Methyl 2-methyl-3-nitro benzoate 70987-78-9 73183-34-3 75833-38-4, 2-Chloropyrimidine-4-carbonitrile 79099-07-3 80887-01-0, 2-Bromo-5-nitrobenzoyl chloride 86087-23-2 97628-92-7 99724-19-3 102362-98-1, 3,3-Dimethyl-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 109384-19-2, 1-Boc-4-hydroxypiperidine 110073-17-1, Methyl 2-morpholin-4-ylpropionate 110763-09-2 123855-51-6 132873-57-5 142253-55-2 148546-99-0, 1-(3-Aminophenyl)-4-methylpiperazine 170491-63-1 171178-50-0, 2,6-Difluoropyridine-3-carboxylic acid 183946-06-7, 2-Methyl-4-nitro-1-pentafluoroethylbenzene 196932-95-3 230299-53-3 442846-90-4 453560-55-9, 1-Boc-2-(3-nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-61-7, 3,3-Dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-6-nitro-2,3-dihydro-1H-indole 453560-64-0, 2-Methoxy-4-nitro-1-pentafluoroethylbenzene 453560-68-4 453560-72-0, (S)-2-Chloro-N-[4-(2-oxiranylmethoxy-)-3-pentafluoroethylphenyl]nicotinamide 453560-93-5, 1-Methyl-4-[1-methyl-1-(4-nitrophenyl)ethyl]pyridinium 454482-16-7 454482-17-8 618445-84-4 618445-90-2 618445-95-7 618445-98-0 618446-13-2 618446-23-4 618446-48-3 618446-51-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

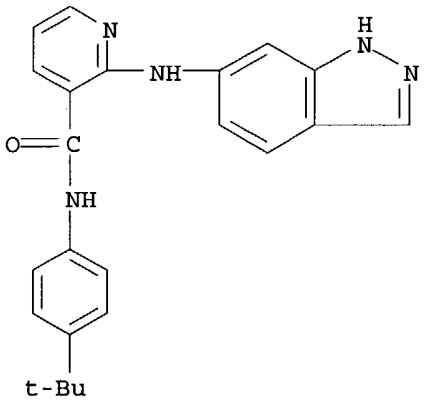
IT 174-66-3P 349-57-5P, 3-Nitro-5-trifluoromethylphenol 393-55-5P, 2-Fluoropyridine-3-carboxylic acid 401-94-5P 619-10-3P, 2-Chloro-5-nitrophenol 695-37-4P, 3-Fluoropyridine 1-oxide 771-99-3P, 4-Phenylpiperidine 774-52-7P, 1-Methyl-4-phenylpiperidine 1073-65-0P, Pyrimidine-4-carboxaldehyde oxime 6310-17-4P 6850-23-3P 6943-17-5P 10043-37-5P 13209-80-8P 13669-28-8P, 1-Methyl-4-methylenepiperidine 17329-31-6P, 6-Amino-3H-quinazolin-4-one 20364-31-2P 20691-89-8P, (1-Methylpiperidin-4-yl)methanol 24252-37-7P, 1-Methylpiperidine-4-carboxylic acid ethyl ester 28286-03-5P 31930-18-4P 40919-12-8P 42182-27-4P 54815-23-5P, 2-(4-Aminophenyl)-2-methylpropionic acid methyl ester 55052-24-9P, 1H-Pyrrolo[2,3-b]pyridine 7-oxide 55052-28-3P, 4-Chloro-1H-pyrrolo[2,3-b]pyridine 56149-31-6P 57841-51-7P 58021-55-9P 58605-12-2P 59115-08-1P, 2-Methyl-2-(4-nitrophenyl)propionic acid methyl ester 59182-61-5P 69296-06-6P, 2-Morpholin-4-ylpropanol 70564-16-8P, 2-Ethyl-4-aminomethylpyridine 72716-86-0P, 4-Cyano-2-methoxypyridine 74728-65-7P, 1-Methyl-6-amino-1H-indazole 76693-04-4P, 4,4-Dimethyl-3,4-dihydro-1H-quinolin-2-one 85160-84-5P, 2,2-Dimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 90221-50-4P, N-(2-Bromo-5-nitrophenyl)acetamide 91133-58-3P 97483-77-7P, 5-Bromopyridine-2-carbonitrile 97509-75-6P 98475-07-1P 103392-84-3P, 2-tert-Butyl-5-nitroaniline 103394-70-3P, 4-tert-Butyl-3-nitrophenylamine 105807-77-0P, 2,2,4-Trimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 105807-84-9P, 6-Amino-2,2-dimethyl-4H-benzo[1,4]oxazin-3-one 106516-27-2P, 3-(1-Methyl-1,2,3,6-tetrahydropyridin-4-yl)-5-nitro-1H-indole 111080-65-0P 111080-66-1P 111196-85-1P, 2-Methyl-2-(4-nitrophenyl)propionic acid 114262-65-6P, 4-(1,1,2,2,3,3,4,4,4-Nonafluorobutyl)phenylamine 117242-06-5P, 4,4-Dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 119899-26-2P, 2-Fluoropyridine-3-carbonyl chloride 125089-58-9P 125089-59-0P 126099-59-0P 136545-11-4P, 2,2-Dimethyl-6-nitro-3,4-dihydro-2H-benzo[1,4]oxazine 137076-22-3P, 1-Boc-4-formylpiperidine 137225-13-9P 140837-70-3P, 3,3-Dimethyl-6-nitro-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 141699-58-3P 142253-56-3P, 1-Boc-3-Hydroxymethylazetidine 142851-03-4P, 1-Boc-Piperidine-4-carboxylic acid ethyl ester 144293-82-3P, 1-(2,2-Dimethyl-6-nitro-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 144293-83-4P, 1-(6-Amino-2,2-dimethyl-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 148900-69-0P, (2-Methoxypyridin-4-

yl)methylamine 149532-90-1P, (2-Methoxypyridin-4-yl)methylamine hydrochloride 150544-04-0P 160726-81-8P 161975-39-9P, 1-Boc-4-Methylsulfonyloxymethylpiperidine 173094-82-1P, 2-(1H-Indazol-6-ylamino)pyridine-3-carboxylic acid 177947-88-5P 179898-72-7P 180692-27-7P, Trifluoromethanesulfonic acid 1-Methyl-1,2,3,6-tetrahydropyridin-4-yl ester 181363-19-9P 182564-38-1P 199296-51-0P 312904-51-1P 327056-62-2P 366452-97-3P 366452-98-4P 408328-42-7P 442846-54-0P, [2-(1-Methylpiperidin-4-yloxy)pyridin-4-yl]methylamine 442846-55-1P, [2-(1-Methylpyrrolidin-2-ylmethoxy)pyridin-4-yl]methylamine 442846-56-2P, (4-Aminomethylpyridin-2-yl)(3-morpholin-4-ylpropyl)amine 442846-58-4P, [2-(1-Methylpiperidin-4-ylmethoxy)pyridin-4-yl]methylamine 442846-59-5P, 3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethylphenylamine 442846-60-8P, 3-(4-Methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenylamine 442846-61-9P, 7-Amino-2-(4-methoxybenzyl)-4,4-dimethyl-3,4-dihydro-2H-isoquinolin-1-one 442846-62-0P, (3-Amino-5-trifluoromethylphenyl)(4-Boc-piperazin-1-yl)methanone 442846-63-1P, 1-(7-Amino-4,4-dimethyl-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-64-2P, 4-tert-Butyl-3-(1-Boc-pyrrolidin-3-ylmethoxy)phenylamine 442846-65-3P, 4-tert-Butyl-3-(1-Boc-azetidin-3-ylmethoxy)phenylamine 442846-67-5P, N-(4-Acetyl-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-68-6P, 2-Fluoro-N-(2,2,4-trimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)nicotinamide 442846-69-7P, N-(2,2-Dimethyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-70-0P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-71-1P, 2-Fluoro-N-(2-Boc-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-72-2P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenyl]nicotinamide 442846-73-3P, 2-Fluoro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-74-4P 442846-75-5P, 2-Fluoro-N-[3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-76-6P, N-(2-Acetyl-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-fluoronicotinamide 442846-77-7P, N-[3,3-Dimethyl-1-(1-methylpiperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-fluoronicotinamide 442846-78-8P, 2-Fluoro-N-[3-(1-Boc-azetidin-3-ylmethoxy)-5-trifluoromethylphenyl]nicotinamide 442846-79-9P, (S)-N-[4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)phenyl]-2-fluoronicotinamide 442846-80-2P, 2-Chloro-N-[2-(4-methoxybenzyl)-4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl]nicotinamide 442846-81-3P, 2-Chloro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-82-4P, 2-[3-[(2-Chloropyridine-3-carbonyl)amino]phenyl]-2-methylpropionic acid methyl ester 442846-83-5P, N-[4-tert-Butyl-3-[2-(1-Boc-piperidin-4-yl)ethyl]phenyl]-2-chloronicotinamide 442846-84-6P 442846-85-7P 442846-86-8P 442846-87-9P 442846-88-0P, 1-[2-(2-tert-Butyl-5-nitrophenoxy)ethyl]piperidine 442846-89-1P, 3,3-Dimethyl-1-(1-methylpiperidin-4-yl)-6-nitro-2,3-dihydro-1H-indole 442846-91-5P, 1-(4,4-Dimethyl-7-nitro-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-92-6P, 2-Bromo-N-(4-methoxybenzyl)-5-nitrobenzamide 442846-93-7P, 4,4-Dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 442846-94-8P, 1-Boc-4-(3-nitro-5-trifluoromethylbenzyl)piperazine 442846-96-0P 442846-97-1P, 1-Methyl-4-[1-methyl-1-(4-nitrophenyl)ethyl]pyridinium iodide 442846-98-2P, 1-Methyl-4-(4-nitrobenzyl)-1,2,3,6-tetrahydropyridine 442846-99-3P 442847-02-1P 442847-03-2P 442847-04-3P, [3-[3-Amino-5-(trifluoromethyl)phenyl]propyl]dimethylamine 442847-06-5P, 4-(2-tert-Butyl-5-nitrophenyl)pyridine 442847-08-7P, 4-tert-Butyl-3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)aniline 442847-11-2P, -2-tert-Butyl-5-nitrophenol 443729-67-7P 452929-03-2P, 1-(2-tert-Butylphenyl)-4-methylpiperazine 453560-49-1P, 1-Boc-4-(3-nitro-5-trifluoromethylphenoxy)piperidine 453560-50-4P, 1-Boc-4-(3-amino-5-trifluoromethylphenoxy)piperidine 453560-51-5P, (S)-4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)phenylamine 453560-52-6P 453560-54-8P, 2-(3-Nitro-5-trifluoromethylphenoxymethyl)pyr

rolidine 453560-56-0P, 1-Methyl-2-(3-nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-57-1P, N-(3-Bromo-5-trifluoromethylphenyl)acetamide 453560-58-2P 453560-59-3P 453560-60-6P, 3,3-Dimethyl-6-nitro-1-piperidin-4-ylmethyl-2,3-dihydro-1H-indole 453560-62-8P 453560-63-9P, 5-Nitro-2-pentafluoroethylphenol 453560-66-2P 453560-67-3P 453560-69-5P 453560-70-8P 453560-73-1P 453560-74-2P, 5-Nitro-2-trifluoromethylanisole 453560-76-4P 453560-77-5P 453560-78-6P, 2-Dimethylamino-1-(3,3-dimethyl-6-nitro-2,3-dihydroindol-1-yl)ethanone 453560-79-7P 453560-80-0P, 2-Boc-4,4-dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 453560-81-1P 453560-82-2P, 2-(4-Methoxybenzyl)-4,4-dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 453560-83-3P, 2-Bromomethyl-4-nitro-1-pentafluoroethylbenzene 453560-84-4P 453560-85-5P 453560-86-6P, (4-Boc-piperazin-1-yl)(3-nitro-5-trifluoromethylphenyl)methanone 453560-88-8P 453560-89-9P, 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-5-trifluoromethylphenylamine 453560-90-2P, 1-Boc-3-(3-nitro-5-trifluoromethylphenoxymethyl)azetidine 453560-91-3P, 2-Bromo-N-(2-hydroxy-5-nitrophenyl)-2-methylpropionamide 453560-92-4P, 4-[1-(2-Bromo-4-nitrophenyl)-1-methylethyl]-1-methylpyridinium iodide 453560-94-6P, 4-[1-(2-Bromo-4-nitrophenyl)-1-methylethyl]-1-methyl-1,2,3,6-tetrahydropyridine 453560-95-7P, 4-(2-tert-Butyl-5-nitrophenyl)-but-3-en-1-ol 453560-96-8P, 4-(2-tert-Butyl-5-nitrophenyl)-but-3-enal 453560-97-9P, 1-[4-(2-tert-Butyl-5-nitrophenyl)-but-3-enyl]pyrrolidine 453562-51-1P, [2-[4-(tert-Butyl)-2-aminophenoxy]ethyl]dimethylamine 453562-53-3P, 1-[2-(tert-Butyl)-5-aminophenyl]-4-methylpiperazine 453562-54-4P, 1-[2-(tert-Butyl)-5-nitrophenyl]-4-methylpiperazine 453562-59-9P 453562-60-2P 453562-67-9P, N-(2-Bromo-5-nitrophenyl)-N-(2-methylprop-2-enyl)acetamide 453562-68-0P, 1-(3,3-Dimethyl-6-nitro-2,3-dihydroindol-1-yl)ethanone 453562-71-5P, 1-Acetyl-6-amino-3,3-dimethylindoline 453562-79-3P, 4-(1,1-Dimethyl-3-morpholin-4-ylpropyl)phenylamine 453562-88-4P 453562-90-8P, 4-(tert-Butyl)-3-(3-piperidylpropyl)phenylamine 453562-95-3P, 1-(2-Morpholin-4-ylethyl)indol-6-ylamine 453563-09-2P 454482-05-4P 454482-07-6P
454482-08-7P 454482-09-8P, 4-(tert-Butyl)-2-(4-methylpiperazinyl)phenylamine 454482-10-1P 454482-11-2P 454482-12-3P 454482-13-4P, 3-(3-Aminophenyl)-1-(4-methylpiperazinyl)propan-1-one 454482-14-5P 454482-15-6P, 1-(2-Pyridyl)pyrrolidin-3-ylamine 561297-73-2P 561297-74-3P 561297-75-4P 561297-76-5P 561297-77-6P 561297-78-7P 561297-79-8P 561297-80-1P 561297-81-2P 561297-82-3P 561297-83-4P 561297-84-5P 561297-85-6P 561297-86-7P 561297-87-8P 561297-88-9P 561297-89-0P 561297-90-3P 561297-91-4P 561297-96-9P 561297-98-1P 561297-99-2P 561298-01-9P 618445-80-0P 618445-81-1P 618445-82-2P 618445-83-3P 618445-85-5P 618445-86-6P 618445-87-7P 618445-92-4P 618445-99-1P 618446-00-7P 618446-01-8P 618446-02-9P 618446-03-0P 618446-04-1P 618446-05-2P 618446-06-3P 618446-07-4P 618446-08-5P 618446-09-6P 618446-10-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT 618446-11-0P 618446-12-1P 618446-14-3P 618446-15-4P 618446-16-5P 618446-17-6P 618446-18-7P 618446-19-8P 618446-20-1P 618446-21-2P 618446-22-3P 618446-24-5P 618446-25-6P 618446-26-7P 618446-27-8P 618446-28-9P 618446-29-0P 618446-30-3P, 2-(2,2,2-Trifluoroethoxy)isonicotinonitrile 618446-31-4P 618446-32-5P 618446-33-6P 618446-34-7P 618446-35-8P 618446-36-9P 618446-37-0P 618446-38-1P 618446-39-2P 618446-40-5P 618446-41-6P 618446-42-7P 618446-43-8P 618446-44-9P 618446-45-0P 618446-46-1P 618446-47-2P 618446-49-4P 618446-50-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)

IT **454480-74-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminopyridinecarboxamides for therapeutic use in treatment of **angiogenesis** mediated diseases such as cancer)
RN 454480-74-1 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-(1H-indazol-6-ylamino)- (9CI) (CA INDEX NAME)



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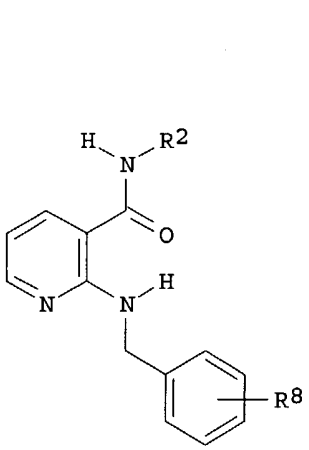
ED Entered STN: 18 Jul 2003
TI Preparation of substituted arylamine derivatives as antitumor agents
IN **Elbaum, Daniel**; Askew, Benny; Booker, Shon; **Germain, Julie**; Habgood, Gregory; Handley, Michael; **Kim, Tae-Seong**; Li, Aiwen; Nishimura, Nobuko; **Patel, Vinod F.**; **Yuan, Chester Chenguang**; **Kim, Joseph L.**
PA **Amgen Inc., USA**
SO U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 46,526.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07D417-02
ICS C07D413-02; C07D043-02; C07D041-02; A61K031-55; A61K031-541; A61K031-5377; A61K031-496; A61K031-4439; A61K031-4545
NCL 514210200; 514217040; 514227800; 514235500; 514253130; 514318000; 514336000; 540597000; 544060000; 546268100
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003134836	A1	20030717	US 2002-197960	20020717 <--
US 2002147198	A1	20021010	US 2002-46526	20020110 <--
WO 2004007457	A2	20040122	WO 2003-US22276	20030715

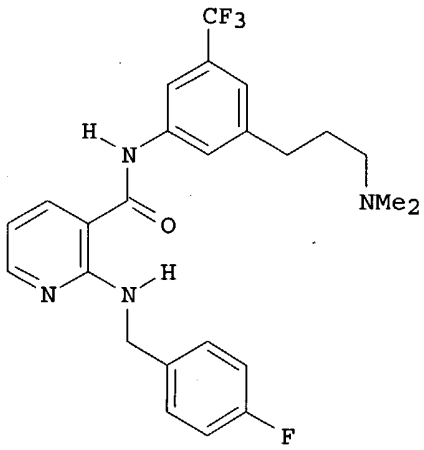
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-261360P P 20010112 <--
US 2001-323686P P 20010919
US 2002-46526 A2 20020110
US 2002-197960 A 20020717
OS MARPAT 139:117339
GI



I



II

AB The title compds. I [R2 = (un)substituted Ph, 9-10 membered bicyclic and 11-14 membered tricyclic (un)saturated heterocyclyl; R8 = halo, NH2, NO2, etc.], and their pharmaceutically acceptable derivs., are prepared and disclosed as agents effective for prophylaxis and treatment of diseases, such as **angiogenesis** mediated diseases. E.g., a multi-step synthesis of II, starting from 1-dimethylamino-2-propyne and 3-bromo-5-trifluoromethylaniline, was given. Selected compds. of the invention, e.g., II, inhibited VEGF-stimulated cell proliferation at a level below 50 nM. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like.

ST arylamine prepn antitumor **angiogenesis** inhibitor; pyridinecarboxamide amino prepn antitumor VEGF inhibitor

IT Cytotoxic agents
(antimetabolites; preparation of substituted aminopyridines for treating cancer in combination with other agents)

IT Eye, disease
(diabetic retinopathy, treatment of; preparation of substituted aminopyridines as antitumor agents)

IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hormone-type agents; preparation of substituted aminopyridines for treating cancer in combination with other agents)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interferon-type agents; preparation of substituted aminopyridines for treating cancer in combination with other agents)

IT **Angiogenesis**
Angiogenesis inhibitors
Antitumor agents
Human
Neoplasm

(preparation of substituted aminopyridines as antitumor agents)
IT Alkylating agents, biological
Antibiotics
Immunomodulators
(preparation of substituted aminopyridines for treating cancer in combination with other agents)
IT Cell proliferation
(treatment of related disorders; preparation of substituted aminopyridines as antitumor agents)
IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VEGFR-2, treatment of related disorders; preparation of substituted aminopyridines as antitumor agents)
IT 393-55-5P 6310-17-4P 20691-89-8P 54815-23-5P 105807-84-9P
144293-82-3P 179898-72-7P 180692-27-7P 375853-85-3P 442846-54-0P
442846-55-1P 442846-56-2P 442846-57-3P 442846-58-4P 442846-59-5P
442846-60-8P 442846-61-9P 442846-62-0P 442846-63-1P 442846-64-2P
442846-65-3P 442846-66-4P 442846-67-5P 442846-68-6P 442846-69-7P
442846-70-0P 442846-71-1P 442846-72-2P 442846-73-3P 442846-74-4P
442846-75-5P 442846-76-6P 442846-77-7P 442846-78-8P 442846-79-9P
442846-80-2P 442846-81-3P 442846-82-4P 442846-83-5P 442846-84-6P
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442846-90-4P 442846-91-5P 442846-92-6P 442846-93-7P 442846-94-8P
442846-95-9P 442846-96-0P 442846-97-1P 442846-98-2P 442846-99-3P
442847-00-9P 442847-01-0P 442847-02-1P 442847-03-2P 442847-04-3P
442847-05-4P 442847-06-5P 442847-07-6P 442847-08-7P 442847-09-8P
442847-10-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted aminopyridines as antitumor agents)
IT 561297-65-2P 561297-67-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted aminopyridines as antitumor agents)
IT 561297-60-7P 561297-61-8P 561297-62-9P 561297-63-0P 561297-64-1P
561297-66-3P 561297-68-5P 561297-69-6P 561297-70-9P 561297-71-0P
561297-72-1P **561298-02-0P 561298-03-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted aminopyridines as antitumor agents)
IT 75-89-8, 2,2,2-Trifluoroethanol 100-52-7, Benzaldehyde, reactions
100-82-3, 3-Fluorobenzylamine 102-28-3, 3'-Aminoacetanilide 106-47-8,
4-Chloroaniline, reactions 106-52-5, 4-Hydroxy-1-methylpiperidine
111-77-3 123-75-1, Pyrrolidine, reactions 139-59-3, 4-Phenoxyaniline
140-75-0, 4-Fluorobenzylamine 372-47-4, 3-Fluoropyridine 372-48-5,
2-Fluoropyridine 456-64-4 555-21-5, 4-Nitrophenylacetonitrile
624-28-2, 2,5-Dibromopyridine 722-92-9 769-92-6, 4-tert-Butylaniline
1083-48-3, 4-(4-Nitrobenzyl)pyridine 1445-73-4, 1-Methyl-piperidin-4-one
1458-98-6, 3-Bromo-2-methylpropene 1462-86-8, 3-Aminopicolinic acid
1692-15-5, 4-Pyridylboronic acid 2008-75-5, 1-(2-Chloroethyl)piperidine
hydrochloride 2393-23-9, 4-Methoxybenzylamine 2620-50-0,
1,3-Benzodioxole-5-methanamine 3282-56-2 3350-78-5,
3,3-Dimethylacryloyl chloride 3554-65-2 4535-90-4 4920-79-0,
2-Chloro-4-nitroanisole 5332-96-7, 1-(4-Nitrophenyl)propan-2-one
5600-21-5, 2-Amino-4-chloro-6-methylpyrimidine 6146-52-7, 5-Nitroindole
6310-21-0, 2-tert-Butylaniline 6313-33-3, Formamidine hydrochloride
7223-38-3, 1-Dimethylamino-2-propyne 10403-47-1, 2-Bromo-5-nitroaniline
19727-83-4, 6-Nitroindoline 19910-33-9, 2-(4-Nitrophenyl)propionic acid
33252-30-1, 2-Chloro-4-cyanopyridine 49609-84-9, 2-Chloropyridine-3-carbonyl chloride 51149-08-7, 3,6-Dichloropyridazine-4-carboxylic acid

54962-75-3, 3-Bromo-5-trifluoromethylaniline 59115-08-1 59382-59-1, Methyl 2-methyl-3-nitrobenzoate 80887-01-0, 2-Bromo-5-nitrobenzoyl chloride 117242-06-5 132873-57-5 137076-22-3, N-tert-Butoxycarbonyl-4-formylpiperidine 142253-57-4 202865-68-7, 3-Bromo-4-fluorobenzylamine hydrochloride 442847-11-2 442847-12-3 442847-13-4 442847-14-5 442847-15-6 442847-16-7 442847-17-8 442847-18-9 442847-19-0 442847-20-3 442847-21-4 442847-22-5 453560-94-6 561298-00-8 561298-01-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted aminopyridines as antitumor agents)

IT 695-37-4P 3276-37-7P 13209-80-8P 20364-31-2P 90221-50-4P 97509-75-6P 106516-27-2P 125089-58-9P 125089-59-0P 126099-59-0P 137225-13-9P 182564-38-1P 255060-77-6P 312904-51-1P 366452-97-3P 366452-98-4P 453560-61-7P 453560-88-8P 453562-54-4P 453562-59-9P 453562-60-2P 453562-67-9P 453562-68-0P 453562-71-5P 454482-06-5P 454482-07-6P 561297-73-2P 561297-74-3P 561297-75-4P 561297-76-5P 561297-77-6P 561297-78-7P 561297-79-8P 561297-80-1P 561297-81-2P 561297-82-3P 561297-83-4P 561297-84-5P 561297-85-6P 561297-86-7P 561297-87-8P 561297-88-9P 561297-89-0P 561297-90-3P 561297-91-4P 561297-93-6P 561297-96-9P 561297-97-0P 561297-98-1P 561297-99-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted aminopyridines as antitumor agents)

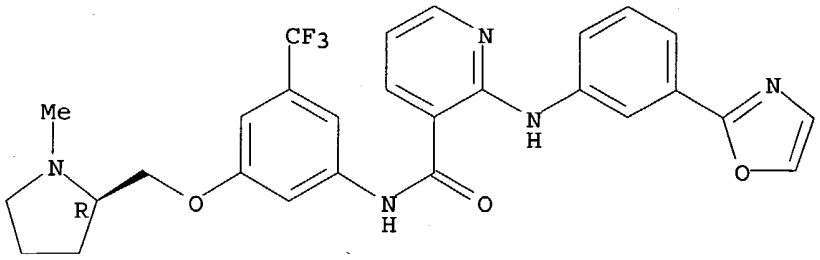
IT 442845-74-1P 442845-77-4P 442846-13-1P 442846-17-5P 442846-22-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of substituted aminopyridines as antitumor agents)

IT 442845-71-8P 442845-72-9P 442845-73-0P 442845-75-2P 442845-76-3P 442845-78-5P 442845-79-6P 442845-80-9P 442845-81-0P 442845-82-1P 442845-83-2P 442845-84-3P 442845-85-4P 442845-86-5P 442845-87-6P 442845-88-7P 442845-89-8P 442845-90-1P 442845-91-2P 442845-92-3P 442845-93-4P 442845-94-5P 442845-95-6P 442845-96-7P 442845-97-8P 442845-98-9P 442845-99-0P 442846-00-6P 442846-01-7P 442846-02-8P 442846-03-9P 442846-04-0P 442846-05-1P 442846-06-2P 442846-07-3P 442846-08-4P 442846-09-5P 442846-10-8P 442846-11-9P 442846-12-0P 442846-14-2P 442846-15-3P 442846-16-4P 442846-18-6P 442846-19-7P 442846-20-0P 442846-21-1P 442846-23-3P 442846-24-4P 442846-25-5P 442846-26-6P 442846-27-7P 442846-28-8P 442846-29-9P 442846-30-2P 442846-31-3P 442846-32-4P 442846-33-5P 442846-34-6P 442846-35-7P 442846-36-8P 442846-37-9P 442846-38-0P 442846-39-1P 442846-40-4P 442846-42-6P 442846-44-8P 442847-23-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of substituted aminopyridines as antitumor agents)

IT **561298-02-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted aminopyridines as antitumor agents)

RN 561298-02-0 HCAPLUS
CN 3-Pyridinecarboxamide, N-[3-[[(2R)-1-methyl-2-pyrrolidinyl]methoxy]-5-(trifluoromethyl)phenyl]-2-[[3-(2-oxazolyl)phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L108 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:396459 HCAPLUS
DN 138:401732
ED Entered STN: 23 May 2003
TI Preparation of aminothiadiazoles as antiproliferatives.
IN Zhang, Zaihui; Chopiuk, Gregory B.; Daynard, Timothy S.; Wang, Shisen
PA Can.
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. 6,420,400.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-433
ICS C07D285-14; C07D417-02
NCL 514361000; 548127000
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003096848	A1	20030522	US 2002-144203	20020510 <--
	US 6420400	B1	20020716	US 2000-545237	20000407 <--
PRAI	US 2000-545237	A2	20000407 <--		

OS MARPAT 138:401732
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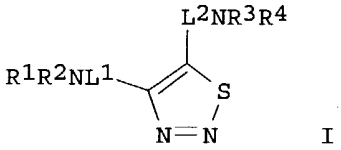

I

AB Title compds. [I; R1-R4 = H, R5, R6, R7; R5 = alkyl, heteroalkyl, aryl, heteroaryl; R6 = (R5)n-alkylene, (R5)n-heteroalkylene, (R5)n-arylene, (R5)n-heteroarylene; R7 = (R6)n-alkylene, (R6)n-heteroalkylene, (R6)n-arylene, (R6)n-heteroarylene; n 0-5; R1R2N, R3R4N = heterocyclyl; L1, L2 = A1A2A3; A1, A2, A3 = bond, alkylene, heteroalkylene, arylene, heteroarylene], were prepared Thus, Me3COK in THF under ice cooling was treated with acetoacetamide and then with PhNCS followed by stirring for 2 h to give a residue which in EtOH was treated with Et3N and then p-tosyl azide followed by stirring for 30 min. at 45° to give 64% 5-phenylamino-1,2,3-thiadiazole-4-carboxamide (KP-15807). The latter at 10 μM in IEC-18 cells reduced cell invasion from 16.8% (controls) to 8%.

ST aminothiadiazole prepn antiproliferative; hyperproliferation treatment aminothiadiazole prepn; cell migration inhibitor aminothiadiazole prepn; apoptosis stimulator aminothiadiazole prepn; neointimal hyperplasia treatment aminothiadiazole prepn; **angiogenesis** inhibitor

aminothiadiazole prepn; lymphoproliferative disorder treatment
aminothiadiazole prepn

IT Neoplasm
(cell growth inhibitors; preparation of aminothiadiazoles as antiproliferatives)

IT Apoptosis
(inducers; preparation of aminothiadiazoles as antiproliferatives)

IT Cell migration
(inhibitors; preparation of aminothiadiazoles as antiproliferatives)

IT Artery, disease
(intima, hyperplasia, treatment; preparation of aminothiadiazoles as antiproliferatives)

IT **Angiogenesis inhibitors**
Antitumor agents
Human
(preparation of aminothiadiazoles as antiproliferatives)

IT Lymphoproliferative disorders
(treatment; preparation of aminothiadiazoles as antiproliferatives)

IT 2039-15-8P 117971-50-3P 149443-19-6P 369605-02-7P 442660-83-5P
442660-90-4P 442660-91-5P 442660-92-6P 442661-23-6P 528855-39-2P
528855-40-5P 528855-41-6P 528855-42-7P 528855-43-8P
528855-44-9P 528855-45-0P 528855-46-1P 528855-47-2P 528855-48-3P
528855-49-4P 528855-50-7P 528855-51-8P 528855-52-9P 528855-53-0P
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528855-61-0P 528855-62-1P 528855-63-2P 528855-64-3P 528855-65-4P
528855-66-5P 528855-67-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminothiadiazoles as antiproliferatives)

IT 103-72-0, Phenyl isothiocyanate 112-71-0, 1-Bromotetradecane 141-78-6, Ethyl acetate, reactions 615-20-3, 2-Chlorobenzothiazole 622-59-3, 4-Methylphenyl isothiocyanate 1544-68-9, 4-Fluorophenyl isothiocyanate 1645-65-4, 4-Trifluoromethylphenyl isothiocyanate 2038-03-1, N-(2-Aminoethyl)morpholine 2131-57-9, 4-Acetylphenyl isothiocyanate 2131-61-5, 4-Nitrophenyl isothiocyanate 3125-64-2, 3-Methoxyphenyl isothiocyanate 3460-49-9, 4-Ethoxyphenyl isothiocyanate 4319-49-7, N-Aminomorpholine 5977-14-0, Acetoacetamide 6590-93-8, 3,5-Dichlorophenyl isothiocyanate 6590-94-9, 3,4-Dichlorophenyl isothiocyanate 6590-96-1, 2,4-Dichlorophenyl isothiocyanate 6590-97-2, 2,3-Dichlorophenyl isothiocyanate 7612-96-6, 4-Phenylazophenyl isothiocyanate 15863-41-9, 4-Methylthiophenyl isothiocyanate 33904-04-0, 3,4-Dimethoxyphenyl isothiocyanate 38985-64-7, 2-Fluorophenyl isothiocyanate 40532-06-7, 2,5-Dimethoxyphenyl isothiocyanate 51333-75-6, 2-Methylthiophenyl isothiocyanate 104968-58-3, 3,5-Dimethoxyphenyl isothiocyanate 139768-71-1 190774-56-2 206761-68-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminothiadiazoles as antiproliferatives)

IT 528855-68-7P 528855-69-8P 528855-70-1P 528855-71-2P 528855-72-3P
528855-73-4P 528855-74-5P 528855-75-6P 528855-76-7P 528855-77-8P
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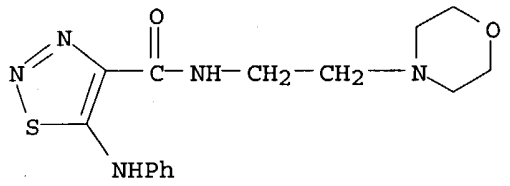
528856-03-3P 528856-04-4P 528856-05-5P 528856-06-6P 528856-07-7P
528856-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminothiadiazoles as antiproliferatives)

IT **528855-40-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminothiadiazoles as antiproliferatives)
RN 528855-40-5 HCAPLUS
CN 1,2,3-Thiadiazole-4-carboxamide, N-[2-(4-morpholinyl)ethyl]-5-(phenylamino)- (9CI) (CA INDEX NAME)



L108 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:676007 HCAPLUS
DN 137:216945
ED Entered STN: 08 Sep 2002
TI Preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases
IN **Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Croghan, Michael; Dipietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Huang, Qi; Kim, Joseph L.; Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Tasker, Andrew ; Xi, Ning; Xu, Shimin; Yuan, Chester Chenguang; Kim, Tae-Seong**
PA **Amgen Inc., USA**
SO PCT Int. Appl., 395 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-00
CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068406	A2	20020906	WO 2002-US3064	20020111 <--
	WO 2002068406	A3	20030424		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003195230	A1	20031016	US 2002-46622	20020110 <--
	EE 200300325	A	20031215	EE 2003-325	20020111 <--
PRAI	US 2001-261882P	P	20010112 <--		
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OS MARPAT 137:216945
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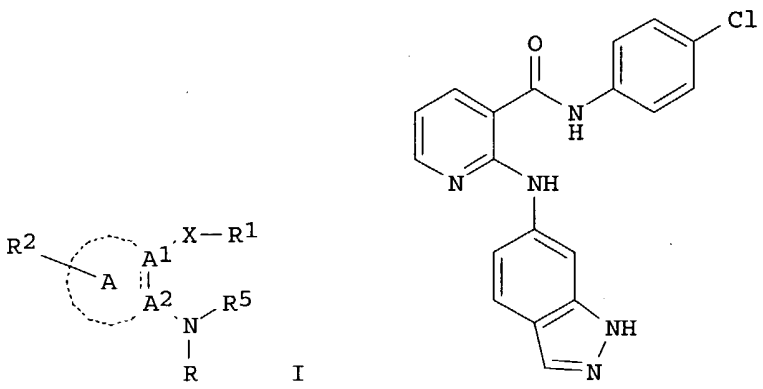

I II

AB The title compds. [I; each of A1 and A2 = C, CH, N; A = 5-6 membered partially saturated heterocyclyl, 5-6 membered heteroaryl, 9-11 membered fused partially saturated heterocyclyl, etc.; X = C(:Z)N(R5a)R4; Z = O, S; R = (un)substituted 4-6 membered heterocyclyl, aryl, fused 9-14 membered bicyclic or tricyclic heterocyclyl; R1 = (un)substituted 6-10 membered aryl, 4-6 membered heterocyclyl, cycloalkyl, etc.; R2 = H, halo, cycloalkyl, etc.; R4 = a bond, alkylene, alkenylene, etc.; R5 = H, alkyl, (un)substituted Ph, aralkyl; R5a is not defined] which are effective for prophylaxis and treatment of diseases, such as **angiogenesis** mediated diseases, were prepared Thus, heating N-(4-chlorophenyl)-2-chloro-3-pyridinecarboxamide with 6-aminoindazole at 150° for 2 h afforded II which inhibited VEGF-stimulated HUVEC proliferation at level below 50 nM. Compds. I showed inhibition of KDR at doses less than 50 μM.

ST indazolylaminonicotinamide prepn KDR **angiogenesis** inhibitor antitumor; nicotinamide indazolylamino prepn KDR **angiogenesis** inhibitor antitumor; vascular endothelial growth factor receptor VEGFR2 KDR indazolylaminonicotinamide prepn

IT Cell proliferation
(inhibitors; preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT **Angiogenesis**
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides as **angiogenesis** inhibitors)

IT Anti-inflammatory agents
Antitumor agents
Human
Inflammation
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT Neoplasm
(treatment of; preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VEGFR-2; preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT **454480-74-1P 454481-03-9P 454481-08-4P**
454481-54-0P 454481-80-2P 454481-82-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT **453564-50-6P 454480-67-2P 454480-68-3P**

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454480-72-9P 454480-73-0P 454480-75-2P
454480-76-3P 454480-77-4P 454480-78-5P
454480-79-6P 454480-80-9P 454480-81-0P
454480-82-1P 454480-83-2P 454480-84-3P
454480-85-4P 454480-86-5P 454480-87-6P
454480-88-7P 454480-89-8P 454480-90-1P
454480-91-2P 454480-92-3P 454480-93-4P
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454481-01-7P 454481-02-8P 454481-04-0P
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454481-09-5P 454481-10-8P 454481-11-9P
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454481-48-2P 454481-49-3P 454481-50-6P
454481-51-7P 454481-52-8P 454481-53-9P
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454481-70-0P 454481-71-1P 454481-72-2P
454481-73-3P 454481-74-4P 454481-75-5P
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454481-98-2P 454481-99-3P 454482-00-9P
454482-01-0P 454482-02-1P 454482-03-2P
454482-04-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT 67-64-1, Acetone, reactions 106-47-8, 4-Chloroaniline, reactions 106-52-5, 4-Hydroxy-1-methylpiperidine 110-91-8, Morpholine, reactions 111-77-3, 2-(2-Methoxyethoxy)ethan-1-ol 123-00-2, 4-(3-Aminopropyl)morpholine 139-59-3, 4-Phenoxyaniline 372-48-5, 2-Fluoropyridine 580-15-4, 6-Aminoquinoline 722-92-9, [4-[2,2,2-Trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]amine 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1202-00-2, [2-(2-Aminophenoxy)ethyl]dimethylamine 1445-73-4, 1-Methylpiperidin-4-one 1458-98-6, 3-Bromo-2-methylpropene 1692-15-5, 4-Pyridylboronic acid 2008-75-5, 1-(2-Chloroethyl)piperidine hydrochloride 2393-23-9, p-Methoxybenzylamine 2942-59-8, 2-Chloronicotinic acid 3282-56-2, 1-tert-Butyl-4-nitrobenzene 3554-65-2, (1-Methylpyrrolidin-2-yl)methanol 4535-90-4 6146-52-7, 5-Nitroindole 6310-21-0, 2-tert-Butylaniline 6967-12-0, 6-Aminoindazole 7223-38-3, 1-(Dimethylamino)-2-propyne 10403-47-1, 2-Bromo-5-nitroaniline 19727-83-4, 6-Nitroindoline

33252-30-1, 2-Chloro-4-cyanopyridine 49609-84-9, 2-Chloronicotinoyl chloride 53062-99-0 54962-75-3, 3-Bromo-5-trifluoromethylaniline 56149-31-6 57841-51-7 58021-55-9 59115-08-1, 2-Methyl-2-(4-nitrophenyl)propionic acid methyl ester 74728-65-7, 1-Methyl-6-amino-1H-indazole 79099-07-3, N-tert-Butoxycarbonylpiperidin-4-one 80887-01-0, 2-Bromo-5-nitrobenzoyl chloride 114262-65-6, (4-(1,1,2,2,3,3,4,4,4-Nonafluorobutyl)phenyl)amine 117242-06-5, 4,4-Dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 132873-57-5 137076-22-3, N-tert-Butoxycarbonyl-4-formylpiperidine 148546-99-0, 1-(5-Aminophenyl)-4-methylpiperazine 173094-82-1, 2-(1H-Indazol-6-ylamino)pyridine-3-carboxylic acid 442847-11-2, 2-tert-Butyl-5-nitrophenol 453560-86-6, (4-Boc-piperazin-1-yl)(3-nitro-5-trifluoromethylphenyl)methanone 453560-89-9, [3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-5-trifluoromethylphenyl]amine 453562-51-1, [2-[4-(tert-Butyl)-2-aminophenoxy]ethyl]dimethylamine 453562-53-3, 1-[2-tert-Butyl-5-aminophenyl]-4-methylpiperazine 453562-79-3, [4-(1,1-Dimethyl-3-(morpholin-4-yl)propyl)phenyl]amine 453562-90-8, 4-(Tert-Butyl)-3-(3-piperidylpropyl)phenylamine 453562-95-3, (1-(2-(Morpholin-4-yl)ethyl)indol-6-yl)amine 453563-09-2 **454481-81-3** 454482-09-8, 4-(tert-Butyl)-2-(4-methylpiperazinyl)phenylamine 454482-10-1 454482-11-2 454482-12-3, 4-(1-Methyl-4-piperidinyl)phenylamine 454482-13-4, 3-(3-Aminophenyl)-1-(4-methylpiperazinyl)propan-1-one 454482-14-5 454482-15-6, [1-(2-Pyridyl)pyrrolidin-3-yl]amine 454482-16-7 454482-17-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

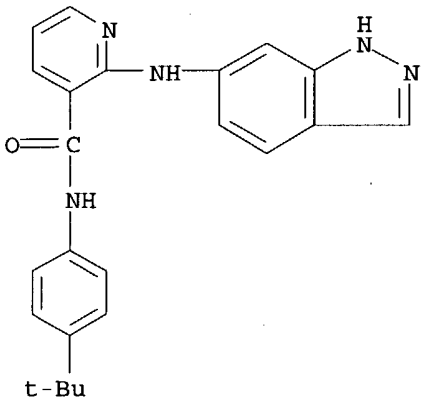
IT 393-55-5P, 2-Fluoronicotinic acid 6310-17-4P, 2-Bromo-1-tert-butyl-4-nitrobenzene 20691-89-8P, (1-Methylpiperidin-4-yl)methanol 54815-23-5P, 2-(4-Aminophenyl)-2-methylpropionic acid methyl ester 90221-50-4P 105807-84-9P, 6-Amino-2,2-dimethyl-4H-benzo[1,4]oxazin-3-one 106516-27-2P 144293-82-3P, 1-(2,2-Dimethyl-6-nitro-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 144293-83-4P, 1-(6-Amino-2,2-dimethyl-2,3-dihydro-benzo[1,4]oxazin-4-yl)ethanone 177947-88-5P 179898-72-7P, 3,3-Dimethyl-6-nitroindoline 180692-27-7P 182564-38-1P 255060-77-6P 442846-54-0P 442846-55-1P 442846-56-2P 442846-58-4P 442846-59-5P 442846-60-8P 442846-61-9P, 7-Amino-2-(4-methoxybenzyl)-4,4-dimethyl-3,4-dihydro-2H-isoquinolin-1-one 442846-62-0P 442846-63-1P, 1-(7-Amino-4,4-dimethyl-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-64-2P 442846-65-3P 442846-67-5P 442846-68-6P 442846-69-7P 442846-70-0P 442846-71-1P 442846-72-2P 442846-73-3P 442846-74-4P 442846-75-5P 442846-76-6P 442846-77-7P 442846-78-8P 442846-79-9P 442846-80-2P 442846-81-3P 442846-82-4P 442846-83-5P 442846-84-6P 442846-85-7P 442846-86-8P 442846-87-9P 442846-88-0P, 1-[2-(2-tert-Butyl-5-nitrophenoxy)ethyl]piperidine 442846-89-1P, 3,3-Dimethyl-1-(1-methylpiperidin-4-yl)-6-nitro-2,3-dihydro-1H-indole 442846-90-4P 442846-91-5P, 1-(4,4-Dimethyl-7-nitro-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-92-6P, 2-Bromo-N-(4-methoxybenzyl)-5-nitrobenzamide 442846-93-7P, 4,4-Dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 442846-94-8P, 1-Boc-4-(3-nitro-5-trifluoromethylbenzyl)piperazine 442846-98-2P, 1-Methyl-4-(4-nitrobenzyl)-1,2,3,6-tetrahydro-pyridine 442847-02-1P 442847-03-2P 442847-04-3P 442847-06-5P, 4-(2-tert-Butyl-5-nitrophenyl)pyridine 442847-07-6P 442847-08-7P, 4-tert-Butyl-3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)aniline 452929-03-2P, 1-[2-tert-Butylphenyl]-4-methylpiperazine 453560-51-5P 453560-61-7P 453560-62-8P 453560-87-7P 453560-88-8P 453562-54-4P, 1-[2-tert-Butyl-5-nitrophenyl]-4-methylpiperazine 453562-59-9P 453562-60-2P 453562-67-9P 453562-68-0P, 1-(3,3-Dimethyl-6-nitro-2,3-dihydro-indol-1-yl)ethanone 454482-05-4P, 2-(6-Quinolylamino)pyridine-3-carboxylic acid 454482-06-5P 454482-07-6P **454482-08-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

IT **454480-74-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 2-(1H-indazol-6-ylamino)nicotinamides for treating KDR-related diseases)

RN 454480-74-1 HCAPLUS

CN 3-Pyridinecarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-2-(1H-indazol-6-ylamino)- (9CI) (CA INDEX NAME)



L108 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:658116 HCAPLUS

DN 137:201332

ED Entered STN: 30 Aug 2002

TI Preparation of heterocyclylalkylamine derivatives as remedies for **angiogenesis** mediated diseases

IN **Chen, Guoqing**; **Adams, Jeffrey**; **Bemis, Jean**; Booker, Shon; Cai, Guolin; **Croghan, Michael**; **Dipietro, Lucian**; **Dominguez, Celia**; **Elbaum, Daniel**; **Germain, Julie**; Geuns-meyer, Stephanie; Handley, Michael; **Huang, Qi**; **Kim, Joseph L.**; **Kim, Tae-seong**; Kiselyov, Alexander; **Ouyang, Xiaohu**; **Patel, Vinod F.**; **Smith, Leon M.**; Stec, Markian; **Tasker, Andrew**; **Xi, Ning**; **Xu, Shimin**; **Yuan, Chester Chenguang**

PA **Amgen Inc., USA**

SO PCT Int. Appl., 502 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D409-12
ICS C07D409-14; C07D213-82; C07D401-12; C07D401-14; C07D409-04; C07D413-14; C07D417-14; C07D405-14; C07D405-12

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002066470	A1	20020829	WO 2002-US743	20020111 <--

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003125339 A1 20030703 US 2002-46681 20020110 <--
BR 2002006435 A 20030923 BR 2002-6435 20020111 <--
EP 1358184 A1 20031105 EP 2002-717325 20020111 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
EE 200300324 A 20031215 EE 2003-324 20020111 <--
NO 2003003181 A 20030911 NO 2003-3181 20030711 <--
PRAI US 2001-261339P P 20010112 <--
US 2001-323764P P 20010919
US 2002-46681 A 20020110
WO 2002-US743 W 20020111
OS MARPAT 137:201332

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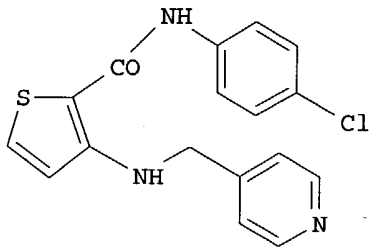

II

AB Title compds. [I; A1, A2 independently = C, N; A = 5-, or 6-membered partially saturated heterocyclyl, 5-, or 6-membered heterocyclyl, 9-, or 10-membered fused partially saturated heterocyclyl, 9-, 10-, or 11-membered fused heteroaryl, naphthyl, 4-, 5-, or 6-membered cycloalkenyl; X = C:ZNR3, C:ZN(R3)R4; Z = O, S; Y = N:CH, NR5(CR6R7), R8N(R5)(CR6R7), NR5(CR6R7)R8; R = 5-, or 6-membered (un)substituted heterocyclyl, 9-, 10-, 11-membered heterocyclyl; R1 = 6-10-membered (un)substituted aryl, 5-, or 6-membered (un)substituted heterocyclyl, 9-11 membered (un)substituted fused heterocyclyl, cycloalkyl, cycloalkenyl; R2 = H, halo, oxo, SH, COOH, CHO; R3 = H, alkyl, 5-, or 6-membered heterocyclyl; R4 = alkylenyl, alkenylenyl, alkynylenyl; R5 = H, alkyl, aralkyl, C6H5; R6, R7 independently = H, halo, CN, alkyl; R6R7 = cycloalkyl; R8 = alkylenyl; etc.] are prepared and are effective for prophylaxis and treatment of diseases, such as **angiogenesis** mediated diseases. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compds. as well as to intermediates useful in such processes. Thus, the title compound II was prepared from Me 3-amino-2-thiophenecarboxylate, 4-chloroaniline, and 4-pyridine carboxaldehyde via coupling reaction.

ST heterocyclylalkylamine prepn remedy **angiogenesis** mediation

disease
IT **Angiogenesis**
Antitumor agents
Cell proliferation
Human
Inflammation
Neoplasm
(preparation of heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)
IT Coupling reaction
(process for preparing heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)
IT Drug delivery systems
(prodrugs; preparation of heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)
IT 453561-03-0P 453561-73-4P 453561-77-8P 453561-95-0P 453562-83-9P
453563-07-0P 453563-37-6P 453563-79-6P 453564-01-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)
IT 352227-57-7P, 2-[(Pyridin-4-ylmethyl)amino]-N-(3-trifluoromethylphenyl)nicotinamide 352227-65-7P 352227-72-6P
352227-74-8P 453560-98-0P 453561-00-7P 453561-01-8P 453561-02-9P
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453561-72-3P 453561-75-6P 453561-76-7P 453561-78-9P 453561-80-3P
453561-81-4P, 2-[(2,3-Dihydrobenzofuran-5-ylmethyl)amino]-N-[3,3-dimethyl-1-(piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]nicotinamide
453561-82-5P 453561-83-6P 453561-84-7P 453561-85-8P,
N-[1-(2-Aminoacetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxypyridin-4-ylmethyl)amino]nicotinamide 453561-86-9P,
N-[1-(2-Aminoacetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-87-0P, (S)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-88-1P, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-89-2P, (R)-N-[3-(Pyrrolidin-2-ylmethoxy)-4-pentafluoroethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-90-5P, (S)-N-[3-(Pyrrolidin-2-ylmethoxy)-5-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-92-7P, N-[3-(Piperidin-4-yloxy)-5-trifluoromethylphenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide
453561-93-8P, N-[4-tert-Butyl-3-[(piperidin-4-yl)methoxy]phenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-94-9P,
N-[4-tert-Butyl-3-(pyrrolidin-2-ylmethoxy)phenyl]-2-[(pyridin-4-ylmethyl)amino]nicotinamide 453561-96-1P 453561-97-2P 453561-98-3P
453561-99-4P 453562-00-0P 453562-02-2P 453562-03-3P 453562-05-5P
453562-07-7P 453562-08-8P 453562-09-9P 453562-10-2P 453562-11-3P
453562-12-4P 453562-13-5P 453562-14-6P 453562-15-7P 453562-16-8P
453562-18-0P 453562-19-1P 453562-20-4P 453562-21-5P 453562-22-6P
453562-23-7P 453562-24-8P 453562-25-9P 453562-26-0P 453562-27-1P

453562-28-2P 453562-29-3P 453562-30-6P 453562-31-7P 453562-32-8P
453562-34-0P 453562-35-1P 453562-36-2P 453562-37-3P 453562-38-4P
453562-39-5P 453562-40-8P 453562-41-9P 453562-42-0P 453562-43-1P
453562-44-2P 453562-45-3P 453562-47-5P 453562-48-6P 453562-49-7P
453562-52-2P 453562-55-5P 453562-56-6P 453562-57-7P 453562-61-3P
453562-62-4P 453562-65-7P 453562-66-8P 453562-69-1P 453562-75-9P
453562-76-0P 453562-80-6P 453562-81-7P 453562-84-0P 453562-85-1P
453562-86-2P 453562-87-3P 453562-91-9P 453562-92-0P 453562-93-1P
453562-94-2P 453562-96-4P 453562-98-6P 453562-99-7P 453563-00-3P
453563-02-5P 453563-06-9P 453563-08-1P 453563-10-5P 453563-11-6P
453563-12-7P 453563-13-8P 453563-14-9P 453563-15-0P 453563-16-1P
453563-17-2P 453563-18-3P 453563-20-7P 453563-21-8P 453563-22-9P
453563-23-0P 453563-24-1P 453563-25-2P 453563-26-3P 453563-27-4P
453563-28-5P 453563-29-6P 453563-32-1P 453563-33-2P 453563-34-3P
453563-35-4P 453563-36-5P 453563-38-7P 453563-39-8P 453563-40-1P
453563-41-2P 453563-42-3P 453563-43-4P 453563-44-5P 453563-45-6P
453563-46-7P 453563-47-8P 453563-48-9P 453563-49-0P 453563-50-3P
453563-51-4P 453563-52-5P 453563-53-6P 453563-54-7P 453563-55-8P
453563-56-9P 453563-57-0P 453563-58-1P 453563-59-2P 453563-60-5P
453563-61-6P 453563-62-7P 453563-63-8P 453563-64-9P 453563-65-0P
453563-66-1P 453563-67-2P 453563-68-3P 453563-69-4P 453563-70-7P
453563-71-8P 453563-72-9P 453563-73-0P 453563-74-1P 453563-75-2P
453563-76-3P 453563-77-4P 453563-78-5P 453563-80-9P 453563-81-0P
453563-82-1P 453563-83-2P 453563-84-3P 453563-85-4P 453563-86-5P
453563-87-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)

IT 453563-88-7P 453563-89-8P 453563-90-1P 453563-91-2P 453563-92-3P
453563-93-4P 453563-94-5P 453563-95-6P 453563-96-7P 453563-97-8P
453563-98-9P 453563-99-0P 453564-00-6P 453564-02-8P 453564-03-9P
453564-04-0P 453564-05-1P 453564-06-2P 453564-07-3P 453564-08-4P
453564-09-5P 453564-10-8P 453564-11-9P 453564-12-0P 453564-13-1P
453564-14-2P 453564-15-3P **453564-16-4P** 453564-17-5P
453564-18-6P 453564-19-7P 453564-20-0P 453564-21-1P 453564-22-2P
453564-23-3P 453564-24-4P 453564-25-5P 453564-26-6P 453564-27-7P
453564-28-8P 453564-30-2P 453564-31-3P 453564-32-4P 453564-33-5P
453564-34-6P 453564-36-8P 453564-37-9P 453564-38-0P 453564-39-1P
453564-40-4P 453564-41-5P 453564-42-6P 453564-43-7P 453564-44-8P
453564-45-9P 453564-46-0P 453564-47-1P 453564-48-2P 453564-49-3P
453564-50-6P 453564-51-7P 453564-52-8P 453564-53-9P
453564-54-0P 453564-55-1P 453564-56-2P 453564-57-3P 453564-58-4P
453564-59-5P 453564-60-8P 453564-61-9P 453564-62-0P 453564-63-1P
453564-64-2P 453564-66-4P 453564-67-5P 453564-68-6P 453564-69-7P
453564-70-0P 453564-71-1P 453564-72-2P 453564-73-3P 453564-74-4P
453564-75-5P 453564-76-6P 453564-77-7P 453564-78-8P 453564-79-9P
453564-80-2P 453564-81-3P 453564-82-4P 453564-83-5P 453564-84-6P
453564-85-7P 453564-86-8P 453564-87-9P 453564-88-0P 453564-89-1P
453564-90-4P 453564-91-5P 453564-92-6P 453564-93-7P 453564-94-8P
453564-95-9P 453564-96-0P 453564-97-1P 453564-98-2P 453564-99-3P
453565-00-9P 453565-01-0P 453565-02-1P 453565-03-2P 453565-04-3P
453565-05-4P 453565-06-5P 453565-07-6P 453565-08-7P 453565-09-8P
453565-10-1P 453565-11-2P 453565-12-3P 453565-13-4P 453565-14-5P
453565-15-6P 453565-16-7P 453565-17-8P 453565-18-9P 453565-19-0P
453565-20-3P 453565-21-4P 453565-22-5P 453565-23-6P 453565-24-7P
453565-25-8P 453565-26-9P 453565-27-0P 453565-28-1P 453565-29-2P
453565-30-5P 453565-31-6P 453565-32-7P 453565-33-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclylalkylamine derivs. as remedies for

angiogenesis mediated diseases)

IT 55-86-7 79-04-9, Chloroacetyl chloride 98-16-8, 3-(Trifluoromethyl)aniline 99-09-2, 3-Nitroaniline 99-57-0, 2-Amino-4-nitrophenol 99-88-7, 4-Isopropylaniline 106-47-8, 4-Chloroaniline, reactions 106-52-5, 4-Hydroxy-1-methylpiperidine 108-01-0, N,N-Dimethylethanolamine 108-23-6, Isopropyl chloroformate 109-01-3, N-Methylpiperazine 109-72-8, Butyllithium, reactions 110-89-4, Piperidine, reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride 123-00-2, 4-Morpholinepropanamine 139-59-3, 4-Phenoxyaniline 288-88-0, 1H-1,2,4-Triazole 328-79-0, 1-Methoxy-3-nitro-5-trifluoromethylbenzene 328-80-3 350-46-9, 1-Fluoro-4-nitrobenzene 372-48-5, 2-Fluoropyridine 527-72-0, 2-Thienylcarboxylic acid 541-41-3, Ethyl chloroformate 609-71-2, 2-Hydroxynicotinic acid 628-13-7, Pyridine hydrochloride 722-92-9, 2-(4-Aminophenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol 769-92-6, 4-tert-Butylaniline 872-85-5, 4-Pyridinecarboxaldehyde 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1118-68-9, Dimethylaminoacetic acid 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 1445-73-4, N-Methyl-4-piperidone 1458-98-6, 3-Bromo-2-methylpropene 1692-15-5, 4-Pyridylboronic acid 1704-62-7, 2-[2-(Dimethylamino)ethoxy]ethanol 2008-75-5, 1-(2-Chloroethyl)piperidine hydrochloride 2221-00-3, (4-Imidazolylphenyl)amine 2435-50-9, Pyrimidine-4-carboxaldehyde 2942-59-8, 2-Chloronicotinic acid 3040-44-6, 2-(Piperid-1-yl)ethanol 3279-07-0, 2-Nitro-4-tert-butylphenol 3282-56-2, 4-tert-Butylnitrobenzene 3438-46-8, 4-Methylpyrimidine 3554-65-2 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 3731-53-1, 4-Aminomethylpyridine 4009-98-7, Methoxymethyltriphenylphosphonium chloride 4160-54-7, 1,3-Dinitro-4-tert-butylbenzene 4769-96-4, 6-Nitroindole 5345-47-1, 2-Aminonicotinic acid 5458-84-4, 2-Iodo-5-nitroanisole 5909-24-0, Ethyl 4-chloro-2-methylthiopyrimidine-5-carboxylate 6146-52-7, 5-Nitroindole 6165-69-1, 3-Thiopheneboronic acid 6310-21-0, 2-tert-Butylaniline 6457-49-4, 4-Piperidylmethanol 7223-38-3, 1-Dimethylamino-2-propyne 10403-47-1, 2-Bromo-5-nitroaniline 13258-63-4, 4-(2-Aminoethyl)pyridine 14446-67-4, 1-Allylpiperidine 19727-83-4, 6-Nitroindoline 19910-33-9, 2-(4-Nitrophenyl)propionic acid 20769-85-1, 2-Bromo-2-methylpropionyl bromide 22288-78-4, Methyl 3-amino-2-thiophenecarboxylate 24424-99-5, Di-tert-butyl dicarbonate 24954-67-4, 2-(4-Nitrophenyl)ethylamine 30529-70-5, 2-Chloro-6-methylnicotinic acid 33252-30-1, 2-Chloro-4-cyanopyridine 54962-75-3, 3-Bromo-5-(trifluoromethyl)phenylamine 57260-71-6, N-Boc-piperazine 60979-14-8, 1-Nitro-4-(1,1,2,2,2-pentafluoroethyl)benzene 71999-74-1 74764-17-3, 2-(2-Pyridylamino)ethylamine 75833-38-4, 2-Chloropyrimidine-4-carbonitrile 80887-01-0, 2-Bromo-5-nitrobenzoyl chloride 102362-98-1, 3,3-Dimethyl-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 105612-50-8 109384-19-2, 1-Boc-4-hydroxypiperidine 110073-17-1, Methyl 2-(morpholin-4-yl)propionate 119899-26-2, 2-Fluoropyridine-3-carbonyl chloride 148546-99-0, 3-(4-Methylpiperazinyl)phenylamine 171178-50-0, 2,6-Difluoropyridine-3-carboxylic acid 183946-06-7, 2-Methyl-4-nitro-1-pentafluoroethylbenzene 201733-56-4 453560-55-9, 1-Boc-2-(3-nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-61-7, 3,3-Dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-6-nitro-2,3-dihydro-1H-indole 453560-62-8 453560-64-0, 2-Methoxy-4-nitro-1-pentafluoroethylbenzene 453560-68-4 453560-72-0, (S)-2-Chloro-N-[4-(2-oxiranylmethoxy)-3-pentafluoroethylphenyl]nicotinamide 453560-93-5, 1-Methyl-4-[1-methyl-1-(4-nitrophenyl)ethyl]pyridinium 453561-19-8 453561-74-5 453563-30-9, 2-Fluoro-N-(4-trifluoromethylphenyl)nicotinamide 453563-31-0, [[2-(1-Isopropylazetidin-3-ylmethoxy)pyridin-4-yl]methyl]amine 453564-35-7, 2-Amino-N-(4-pentafluoroethylphenyl)nicotinamide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylalkylamine derivs. as remedies for **angiogenesis** mediated diseases)

IT 349-57-5P, 3-Nitro-5-trifluoromethylphenol 393-55-5P, 2-Fluoronicotinic

acid 6310-17-4P, 2-Bromo-1-tert-butyl-4-nitrobenzene 6425-46-3P, 4-[(4-Nitrophenyl)methyl]morpholine 13669-28-8P, 1-Methyl-4-methylenepiperidine 16153-81-4P, 4-Methyl-1-(4-aminophenyl)piperazine 16155-03-6P, 4-Methyl-1-(4-nitrophenyl)piperazine 18755-53-8P, 2-Methyl-2-(4-nitrophenyl)propan-1-ol 20691-89-8P, (1-Methylpiperidin-4-yl)methanol 24252-37-7P, 1-Methylpiperidine-4-carboxylic acid ethyl ester 29241-65-4P, 5-Bromo-2-chloronicotinic acid 31951-12-9P 51013-67-3P, 4-(Morpholin-4-ylmethyl)phenylamine 51444-31-6P, 2-(1,2,4-Triazolyl)ethylamine 53062-99-0P 54815-23-5P, 2-(4-Aminophenyl)-2-methylpropionic acid methyl ester 56329-05-6P 57841-51-7P 59115-08-1P, 2-Methyl-2-(4-nitrophenyl)propionic acid methyl ester 60979-04-6P, 4-(1,1,2,2,2-Pentafluoroethyl)phenylamine 69296-06-6P, 2-Morpholin-4-ylpropanol 72716-86-0P, 4-Cyano-2-methoxypyridine 85160-84-5P, 2,2-Dimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 90221-50-4P, N-(2-Bromo-5-nitrophenyl)acetamide 91133-58-3P 94838-59-2P 100973-67-9P 101537-64-8P, 3-[(tert-Butoxy)carbonylamino]thiophene-2-carboxylic acid 103392-84-3P, 2-tert-Butyl-5-nitroaniline 104612-36-4P, 5-Bromo-2-hydroxynicotinic acid 105807-77-0P, 2,2,4-Trimethyl-6-nitro-4H-benzo[1,4]oxazin-3-one 105807-84-9P, 6-Amino-2,2-dimethyl-4H-benzo[1,4]oxazin-3-one 106516-27-2P, 3-(1-Methyl-1,2,3,6-tetrahydropyridin-4-yl)-5-nitro-1H-indole 117242-06-5P, 4,4-Dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 136545-11-4P, 2,2-Dimethyl-6-nitro-3,4-dihydro-2H-benzo[1,4]oxazine 137076-22-3P, 1-Boc-4-formylpiperidine 140837-70-3P, 3,3-Dimethyl-6-nitro-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide 142253-56-3P, 1-Boc-3-Hydroxymethylazetidine 142253-57-4P, Methanesulfonic acid N-Boc-azetidin-3-ylmethyl ester 142851-03-4P, 1-Boc-piperidine-4-carboxylic acid ethyl ester 143094-45-5P, 5-Bromo-2-chloro-N-(4-chlorophenyl)nicotinamide 144226-16-4P 144293-82-3P, 1-(2,2-Dimethyl-6-nitro-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 144293-83-4P, 1-(6-Amino-2,2-dimethyl-2,3-dihydrobenzo[1,4]oxazin-4-yl)ethanone 148900-69-0P, ((2-Methoxy-4-pyridyl)methyl)amine 149532-90-1P, ((2-Methoxypyridin-4-yl)methyl)amine hydrochloride 161975-39-9P, 1-Boc-4-methylsulfonyloxymethylpiperidine 179898-72-7P, 3,3-Dimethyl-6-nitroindoline 180692-27-7P, Trifluoromethanesulfonic acid 1-methyl-1,2,3,6-tetrahydropyridin-4-yl ester 181363-19-9P 182564-38-1P, 3-(1-Methyl-4-piperidyl)indole-5-ylamine 436095-35-1P, 3-[(4-Methylpiperazinyl)sulfonyl]phenylamine 442846-54-0P, [(2-(1-Methylpiperidin-4-yloxy)pyridin-4-yl)methyl]amine 442846-55-1P, [(2-(1-Methylpyrrolidin-2-ylmethoxy)pyridin-4-yl)methyl]amine 442846-56-2P, (4-Aminomethylpyridin-2-yl)(3-morpholin-4-ylpropyl)amine 442846-58-4P, [(2-(1-Methylpiperidin-4-ylmethoxy)pyridin-4-yl)methyl]amine 442846-59-5P, 3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethylphenylamine 442846-60-8P, (3-(4-Methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenyl)amine 442846-61-9P, 7-Amino-2-(4-methoxybenzyl)-4,4-dimethyl-3,4-dihydro-2H-isoquinolin-1-one 442846-62-0P, (3-Amino-5-trifluoromethylphenyl)(4-Boc-piperazin-1-yl)methanone 442846-63-1P, 1-(7-Amino-4,4-dimethyl-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-64-2P, 4-tert-Butyl-3-(1-Boc-pyrrolidin-3-ylmethoxy)phenylamine 442846-65-3P, 4-tert-Butyl-3-(1-Boc-azetidin-3-ylmethoxy)phenylamine 442846-67-5P, N-(4-Acetyl-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-68-6P, 2-Fluoro-N-(2,2,4-trimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)nicotinamide 442846-69-7P, N-(2,2-Dimethyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-fluoronicotinamide 442846-70-0P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-71-1P, 2-Fluoro-N-(2-Boc-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-72-2P, 2-Fluoro-N-[3-(4-methylpiperazin-1-ylmethyl)-4-pentafluoroethylphenyl]nicotinamide 442846-73-3P, 2-Fluoro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-74-4P, 2-Fluoro-N-[3-((4-Boc-piperazin-1-yl)carbonyl)-5-trifluoromethylphenyl]nicotinamide 442846-75-5P, 2-Fluoro-N-[3-(4-Boc-

piperazin-1-ylmethyl)-5-trifluoromethylphenyl]nicotinamide 442846-76-6P, N-(2-Acetyl-4,4-dimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2-fluoronicotinamide 442846-77-7P, N-[3,3-Dimethyl-1-(1-methylpiperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-fluoronicotinamide 442846-78-8P, 2-Fluoro-N-[3-(1-Boc-azetidin-3-ylmethoxy)-5-trifluoromethylphenyl]nicotinamide 442846-79-9P, (S)-N-[4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)phenyl]-2-fluoronicotinamide 442846-80-2P, 2-Chloro-N-[2-(4-methoxybenzyl)-4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl]nicotinamide 442846-81-3P, 2-Chloro-N-(4,4-dimethyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)nicotinamide 442846-82-4P, 2-[3-[(2-Chloropyridine-3-carbonyl)amino]phenyl]-2-methylpropionic acid methyl ester 442846-83-5P, N-[4-tert-Butyl-3-[2-(1-Boc-piperidin-4-yl)ethyl]phenyl]-2-chloronicotinamide 442846-84-6P 442846-85-7P 442846-86-8P 442846-87-9P 442846-88-0P, 1-[2-(2-tert-Butyl-5-nitrophenoxy)ethyl]piperidine 442846-90-4P 442846-91-5P, 1-(4,4-Dimethyl-7-nitro-3,4-dihydro-1H-isoquinolin-2-yl)ethanone 442846-92-6P, 2-Bromo-N-(4-methoxybenzyl)-5-nitrobenzamide 442846-93-7P, 4,4-Dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 442846-94-8P, 1-Boc-4-(3-nitro-5-trifluoromethylbenzyl)piperazine 442846-97-1P, 1-Methyl-4-[1-methyl-1-(4-nitrophenyl)ethyl]pyridinium iodide 442846-98-2P, 1-Methyl-4-(4-nitrobenzyl)-1,2,3,6-tetrahydropyridine 442847-02-1P 442847-03-2P, [3-[3-Amino-5-(trifluoromethyl)phenyl]propyn-2-yl]dimethylamine 442847-04-3P, [3-[3-Amino-5-(trifluoromethyl)phenyl]propyl]dimethylamine 442847-06-5P, 4-(2-tert-Butyl-5-nitrophenyl)pyridine 442847-07-6P 442847-08-7P, 4-tert-Butyl-3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)aniline 442847-11-2P, 2-tert-Butyl-5-nitrophenol 452929-03-2P, 1-(2-tert-Butylphenyl)-4-methylpiperazine 453560-49-1P, 1-Boc-4-(3-nitro-5-trifluoromethylphenoxy)piperidine 453560-50-4P, 1-Boc-4-(3-amino-5-trifluoromethylphenoxy)piperidine 453560-51-5P, (S)-4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)phenylamine 453560-52-6P 453560-53-7P, N-[3-(1-Methylpiperidin-4-yl)-5-trifluoromethylphenyl]-2-fluoronicotinamide 453560-54-8P, 2-(3-Nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-56-0P, 1-Methyl-2-(3-nitro-5-trifluoromethylphenoxymethyl)pyrrolidine 453560-57-1P, N-(3-Bromo-5-trifluoromethylphenyl)acetamide 453560-58-2P 453560-59-3P 453560-60-6P, 3,3-Dimethyl-6-nitro-1-(piperidin-4-ylmethyl)-2,3-dihydro-1H-indole 453560-63-9P, 5-Nitro-2-pentafluoroethylphenol 453560-66-2P 453560-67-3P 453560-69-5P 453560-70-8P 453560-71-9P, (S)-2-Chloro-N-[4-(2-hydroxy-3-(pyrrolidin-1-yl)propoxy)-3-pentafluoroethylphenyl]nicotinamide 453560-73-1P 453560-74-2P, 5-Nitro-2-trifluoromethylanisole 453560-76-4P 453560-77-5P, (R)-2-Chloro-N-[3-(2-hydroxy-2-(pyrrolidin-1-yl)propoxy)-4-pentafluoroethylphenyl]nicotinamide 453560-78-6P, 2-Dimethylamino-1-(3,3-dimethyl-6-nitro-2,3-dihydroindol-1-yl)ethanone 453560-79-7P 453560-80-0P, 2-Boc-4,4-dimethyl-7-nitro-1,2,3,4-tetrahydroisoquinoline 453560-81-1P 453560-82-2P, 2-(4-Methoxybenzyl)-4,4-dimethyl-7-nitro-3,4-dihydro-2H-isoquinolin-1-one 453560-83-3P, 2-Bromomethyl-4-nitro-1-pentafluoroethylbenzene 453560-84-4P 453560-85-5P 453560-86-6P, (4-Boc-piperazin-1-yl)(3-nitro-5-trifluoromethylphenyl)methanone 453560-87-7P 453560-88-8P 453560-89-9P, 3-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-5-trifluoromethylphenylamine 453560-90-2P, 1-Boc-3-(3-nitro-5-trifluoromethylphenoxymethyl)azetidine 453560-91-3P, 2-Bromo-N-(2-hydroxy-5-nitrophenyl)-2-methylpropionamide 453560-92-4P, 4-[1-(2-Bromo-4-nitrophenyl)-1-methylethyl]-1-methylpyridinium iodide 453560-94-6P, 4-[1-(2-Bromo-4-nitrophenyl)-1-methylethyl]-1-methyl-1,2,3,6-tetrahydropyridine 453560-95-7P, 4-(2-tert-Butyl-5-nitrophenyl)but-3-en-1-ol 453560-96-8P, 4-(2-tert-Butyl-5-nitrophenyl)but-3-enal 453560-97-9P, 1-[4-(2-tert-Butyl-5-nitrophenyl)but-3-enyl]pyrrolidine 453560-99-1P 453561-10-9P, 6-Methyl-2-[(4-pyridylmethyl)amino]pyridine-3-carboxylic acid 453561-25-6P, 5-(3-Thiophene)-2-chloro-N-(4-chlorophenyl)nicotinamide 453561-30-3P 453561-31-4P 453562-01-1P,

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453562-54-4P, 1-[2-(tert-Butyl)-5-nitrophenyl]-4-methylpiperazine
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453562-63-5P, 1-(6-Nitroindolinyl)-2-piperidylethan-1-one 453562-64-6P,
1-(2-Piperidylethyl)indoline-6-ylamine 453562-67-9P,
N-(2-Bromo-5-nitrophenyl)-N-(2-methylprop-2-enyl)acetamide 453562-68-0P
453562-71-5P, 1-Acetyl-6-amino-3,3-dimethylindoline 453562-74-8P
453562-77-1P, 2-Methyl-2-(4-nitrophenyl)propionaldehyde 453562-78-2P,
4-[3-Methyl-3-(4-nitrophenyl)butyl]morpholine 453562-79-3P,
4-(1,1-Dimethyl-3-(morpholin-4-yl)propyl)phenylamine 453562-88-4P,
(2E)-3-[2-(tert-Butyl)-5-nitrophenyl]-1-(piperid-1-yl)prop-2-en-1-one
453562-89-5P, (2E)-3-[2-(tert-Butyl)-5-aminophenyl]-1-(piperid-1-yl)prop-2-
en-1-one 453562-90-8P, 4-(tert-Butyl)-3-(3-piperidylpropyl)phenylamine
453562-95-3P, (1-(2-(Morpholin-4-yl)ethyl)indole-6-yl)amine 453563-01-4P
453563-03-6P, 2-[2-[2-(Dimethylamino)ethoxy]ethoxy]pyridine-4-carbonitrile
453563-04-7P 453563-05-8P, N-[4-(tert-Butyl)phenyl]-2-fluoropyridine-3-
carboxamide 453563-09-2P, N-(4-tert-Butylphenyl)-2,6-
difluoronicotinamide 453563-19-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of heterocyclylalkylamine derivs. as remedies for
angiogenesis mediated diseases)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

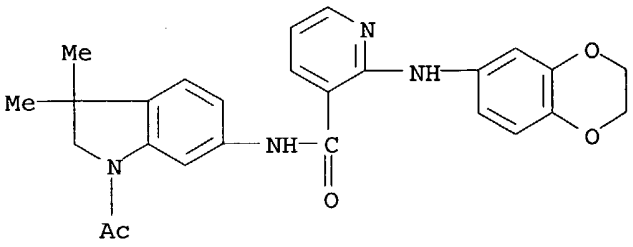
RE

(1) Astrazeneca Uk Limited; WO 0047212 A 2000 HCAPLUS
(2) Eli Lilly And Company; WO 0039111 A 2000 HCAPLUS
(3) Eli Lilly And Company; WO 0039117 A 2000 HCAPLUS
(4) Fujisawa Pharmaceutical Co; WO 9641795 A 1996 HCAPLUS
(5) Fujisawa Pharmaceutical Co Ltd; WO 9824771 A 1998 HCAPLUS
(6) Fujisawa Pharmaceutical Co Ltd; WO 0130745 A 2001 HCAPLUS
(7) Guido, B; JOURNAL OF MEDICINAL CHEMISTRY 2000, V43(12), P2310
(8) Hennequin, L; JOURNAL OF MEDICINAL CHEMISTRY 1999, V42(26), P5369 HCAPLUS
(9) Hoechst Marion Roussel Deutschland Gmbh; WO 0002851 A 2000 HCAPLUS
(10) Kelly, T; US 5532358 A 1996 HCAPLUS
(11) LI, S; JOURNAL OF MEDICINAL CHEMISTRY 1999, V42(25), P5120
(12) Novartis Ag; WO 0027820 A 2000 HCAPLUS
(13) Novartis Ag; WO 0155114 A 2001 HCAPLUS
(14) Novartis Ag; WO 0185691 A 2001 HCAPLUS
(15) Novartis Ag; WO 0185715 A 2001 HCAPLUS
(16) Pfizer Products Inc; WO 9845268 A 1998 HCAPLUS
(17) Schering Aktiengesellschaft; WO 9932477 A 1999 HCAPLUS
(18) Schering Aktiengesellschaft; WO 0027819 A 2000 HCAPLUS
(19) Schiper, E; US 3226394 A 1965 HCAPLUS

IT **453564-16-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of heterocyclylalkylamine derivs. as remedies for
angiogenesis mediated diseases)

RN 453564-16-4 HCAPLUS

CN 3-Pyridinecarboxamide, N-(1-acetyl-2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-
2-[(2,3-dihydro-1,4-benzodioxin-6-yl)amino]- (9CI) (CA INDEX NAME)



L108 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:555470 HCAPLUS
DN 137:125160
ED Entered STN: 26 Jul 2002
TI Preparation of 1,2,4-triazole-3,5-diamine derivatives as kinase inhibitors
IN Lin, Ronghui; Connolly, Peter J.; Wetter, Steven; Huang, Shenlin; Emanual, Stuart; Guninger, Robert; Middleton, Steve
PA Ortho McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D249-14
ICS C07D409-06; C07D405-06; C07D401-06; C07D413-06; C07D417-06; C07D403-12; C07D417-14; C07D409-14; A61K031-4196; A61K031-4439
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002057240	A1	20020725	WO 2001-US50559	20011221 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1355889	A1	20031029	EP 2001-998116	20011221 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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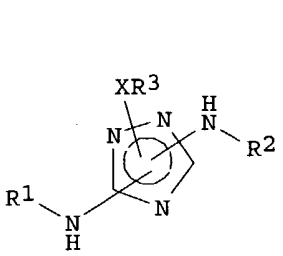
	US 2004077699	A1	20040422	US 2001-29750	20011221 <--
	NO 2003002848	A	20030820	NO 2003-2848	20030620 <--
PRAI	US 2000-257703P	P	20001222 <--		
	WO 2001-US50559	W	20011221		

OS MARPAT 137:125160
GI



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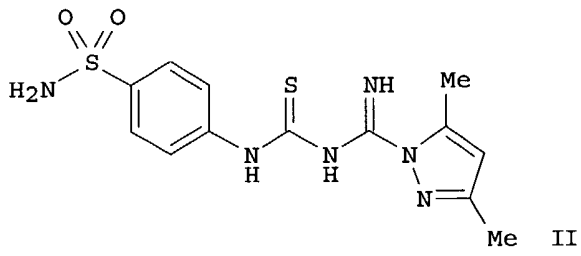

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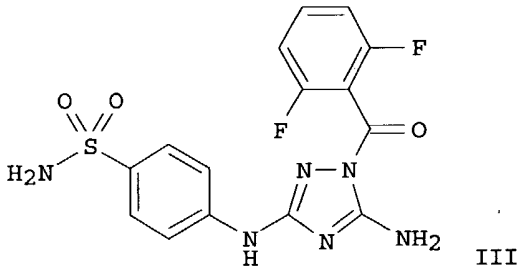

III

AB The title derivs. [I; R1 = (un)substituted C1-8 alkyl, cycloalkyl, heterocyclyl, (hetero)aryl, (un)substituted C1-8 alkoxy, amino, etc.; R2 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, HO(C1-8 alkyl); R3 = C1-8 alkyl, (un)substituted C2-8 alkenyl or alkynyl; (un)substituted cycloalkyl, heterocyclyl, (hetero)aryl, etc.; X = CO, C(:S), SO2] were prepared I and their pharmaceutically acceptable salts are selective kinase or dual-kinase inhibitors useful in the treatment of kinase-mediated disorders, especially as chemotherapeutic agents for treatment of cancer. Thus, adding DMF solution of 4-H2NSO2C6H4N:C:S at 0° to DMF solution of 1-amidino-3,5-dimethylpyrazole nitrate containing NaOH powder and stirring the mixture at 50-60° for 1 h gave the thiourea II. Stirring the latter vigorously with hydrazine for 2-3 h at 50-60° and N-acylating the resulting aminotriazole derivative with 2,6-F2C6H3COCl in pyridine gave a title compound III which inhibited enzymic activity of vascular endothelial growth factor receptor-2 with IC50 0.1062 μM.

ST aminotriazole prepn inhibitor kinase; triazolylaminobenzenesulfonamide amino difluorobenzoyl prepn kinase inhibitor; vascular endothelial growth factor receptor inhibitor triazolediamine deriv prepn

IT Alopecia
Angiogenesis
Antitumor agents
Blood vessel, disease
(preparation of triazolediamine derivs. as kinase inhibitors)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of triazolediamine derivs. as kinase inhibitors)

IT Artery, disease
(restenosis; preparation of triazolediamine derivs. as kinase inhibitors)

IT 98-88-4, Benzoyl chloride 393-52-2, 2-Fluorobenzoyl chloride 527-69-5, 2-Furoyl chloride 610-14-0, 2-Nitrobenzoyl chloride 933-88-0, 2-Methylbenzoyl chloride 938-18-1, 2,4,6-Trimethylbenzoyl chloride 1989-53-3, 2,6-Dimethoxybenzoyl chloride 4136-95-2, 2,4,6-Trichlorobenzoyl chloride 4659-45-4, 2,6-Dichlorobenzoyl chloride 18063-02-0, 2,6-Difluorobenzoyl chloride 60230-36-6, 2,6-Difluorobenzenesulfonyl chloride 72482-64-5, 2,4-Difluorobenzoyl chloride 79455-63-3, 2-Chloro-6-fluorobenzoyl chloride 109227-12-5, 2-Fluoro-6-(trifluoromethyl)benzoyl chloride 189807-20-3, 2,3,6-Trifluorobenzoyl chloride 261762-81-6 261763-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation of triazole derivative; preparation of triazolediamine derivs. as
kinase inhibitors)
IT 1455-77-2, 1H-1,2,4-Triazole-3,5-diamine 3310-68-7 37627-92-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-benzoylation; preparation of triazolediamine derivs. as kinase inhibitors)
IT 18162-48-6, tert-Butyldimethylsilyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-protection of difluorophenylethanol; preparation of triazolediamine derivs. as kinase inhibitors)
IT 38184-47-3, 3,5-Dimethylpyrazole-1-carboxamidine nitrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction with Ph isothiocyanate derivative; preparation of triazolediamine derivs. as kinase inhibitors)
IT 103-71-9, Phenyl isocyanate, reactions 65295-69-4, 2,6-Difluorophenyl isocyanate 207974-17-2, 2,6-Difluorophenyl isothiocyanate
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction with aminotriazole derivative; preparation of triazolediamine
derivs. as kinase inhibitors)
IT 7356-55-0 17614-69-6 223785-90-8 223785-92-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction with carboxamidine derivative; preparation of triazolediamine
derivs. as kinase inhibitors)
IT 23861-85-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction with pyrazolecarboxamidine derivative; preparation of triazolediamine derivs. as kinase inhibitors)
IT 22906-75-8, 1-Amidino-3,5-dimethylpyrazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition with (aminosulfonyl)benzene isothiocyanate; preparation of triazolediamine derivs. as kinase inhibitors)
IT 51908-29-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition with amidinodimethylpyrazole; preparation of triazolediamine derivs.
as kinase inhibitors)
IT 425-75-2, Ethyl trifluoromethanesulfonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of aminotriazole derivative; preparation of triazolediamine derivs.
as kinase inhibitors)
IT 55-22-1, Isonicotinic acid, reactions 59-67-6, Nicotinic acid, reactions 88-13-1, Thiophene-3-carboxylic acid 98-89-5, Cyclohexanecarboxylic acid 98-98-6, Picolinic acid 527-72-0, Thiophene-2-carboxylic acid 632-46-2, 2,6-Dimethylbenzoic acid 1124-65-8, 3-(2-Thienyl)acrylic acid 1460-16-8, Cycloheptanecarboxylic acid 1918-77-0, 2-Thiopheneacetic acid 1918-79-2, 5-Methylthiophene-2-carboxylic acid 3400-45-1, Cyclopentanecarboxylic acid 4066-41-5, 5-Acetylthiophene-2-carboxylic acid 4100-13-4, 1,2,3-Thiadiazole-4-carboxylic acid 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 7311-63-9, 5-Bromothiophene-2-carboxylic acid 7311-64-0, 3-Bromothiophene-2-carboxylic acid 13064-83-0, trans-4-Methyl-1-cyclohexanecarboxylic acid 18212-21-0, 4-Methyl-1,2,3-thiadiazole-5-carboxylic acid 21169-71-1, Isoxazole-5-carboxylic acid 23806-24-8, 3-Methylthiophene-2-carboxylic acid 29212-25-7, 5-tert-Butylthiophene-2-carboxylic acid 32431-84-8, 3-Fluorothiophene-2-carboxylic acid 38289-28-0, trans-4-Butyl-1-cyclohexanecarboxylic acid 50901-18-3, 3-(Acetylamino)thiophene-2-carboxylic acid 53137-27-2, 2,4-Dimethylthiazole-5-carboxylic acid 56586-13-1 59337-89-2, 3-Chlorothiophene-2-carboxylic acid 67595-44-2

74772-17-1 83141-10-0, 2,6-Difluoro-3-nitrobenzoic acid 85068-28-6, 2,6;-Difluorophenylacetic acid 119082-97-2, 5-(2-Pyridyl)thiophene-2-carboxylic acid 139926-23-1, 3-Ethoxythiophene-2-carboxylic acid 152152-09-5, 2,6-Difluorocinnamic acid 207866-53-3 225104-76-7, 3-Chloro-2,6-difluorobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of triazole derivative; preparation of triazolediamine derivs. as kinase inhibitors)

IT 144-83-2 2221-00-3, 4-Imidazol-1-ylaniline 6523-49-5 52761-74-7 53250-82-1 77837-46-8 89518-99-0 90556-91-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation with di-Ph cyanocarbonimidate; preparation of triazolediamine derivs. as kinase inhibitors)

IT 79463-77-7, Diphenyl cyanocarbonimidate
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation with imidazolylaniline; preparation of triazolediamine derivs. as kinase inhibitors)

IT 150977-45-0, Vascular endothelial growth factor receptor-2 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-31-3P 443799-33-5P 443799-38-0P 443799-39-1P 443799-42-6P 443799-46-0P 443799-47-1P 443799-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-benzoylation; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-40-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-methylation; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-49-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation with dimethylthiophenecarboxylic acid; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-45-9P 443799-48-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation with ethylthiophenecarboxylic acid; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-50-6P 443799-51-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation with methylthiophenecarboxylic acid; preparation of triazolediamine derivs. as kinase inhibitors)

IT 443799-44-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation with thiophenecarboxylic acid derivative; preparation of triazolediamine derivs. as kinase inhibitors)

IT 23229-72-3P, 5-Ethyl-2-thiophenecarboxylic acid 65613-27-6P, 3,5-Dimethyl-2-thiophenecarboxylic acid 443799-35-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation with triazole derivative; preparation of triazolediamine

derivs. as kinase inhibitors)
IT 443799-36-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection; preparation of triazolediamine derivs. as kinase
inhibitors)
IT 443799-30-2P 443799-32-4P 443799-37-9P 443799-41-5P 443799-43-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with hydrazine; preparation of triazolediamine derivs.
as kinase inhibitors)
IT 2267-47-2P, Benzenemethanol, 2,4-difluoro-α-methyl-
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and silylation; preparation of triazolediamine derivs. as kinase
inhibitors)
IT 134549-83-0, Protein kinase 347147-98-2, Receptor protein kinase
372092-80-3, Protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of triazolediamine derivs. as kinase inhibitors)
IT 324074-12-6P 324074-15-9P 324074-30-8P 443797-96-4P 443797-97-5P
443797-98-6P 443797-99-7P 443798-00-3P 443798-01-4P 443798-02-5P
443798-03-6P 443798-04-7P 443798-05-8P 443798-06-9P 443798-07-0P
443798-08-1P 443798-09-2P 443798-10-5P 443798-11-6P 443798-12-7P
443798-13-8P 443798-14-9P 443798-15-0P 443798-16-1P 443798-17-2P
443798-18-3P 443798-19-4P 443798-20-7P 443798-21-8P 443798-22-9P
443798-23-0P 443798-24-1P 443798-25-2P 443798-26-3P 443798-27-4P
443798-28-5P 443798-29-6P 443798-30-9P 443798-31-0P 443798-32-1P
443798-33-2P 443798-34-3P 443798-35-4P 443798-36-5P 443798-37-6P
443798-38-7P 443798-39-8P 443798-40-1P 443798-41-2P 443798-42-3P
443798-43-4P 443798-44-5P 443798-45-6P 443798-46-7P 443798-47-8P
443798-48-9P 443798-49-0P 443798-50-3P 443798-51-4P 443798-52-5P
443798-53-6P 443798-54-7P **443798-55-8P** 443798-56-9P
443798-57-0P 443798-58-1P 443798-59-2P 443798-60-5P 443798-61-6P
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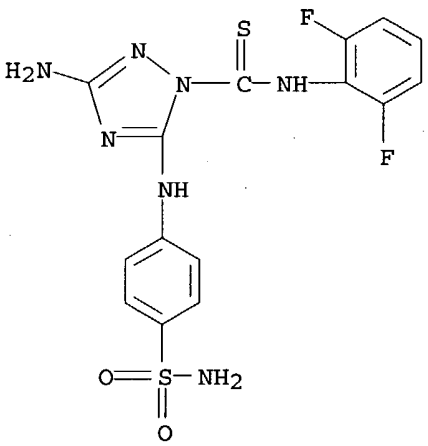
443798-97-8P 443798-98-9P 443798-99-0P 443799-00-6P 443799-01-7P
443799-02-8P 443799-03-9P 443799-04-0P 443799-05-1P 443799-06-2P
443799-07-3P 443799-08-4P 443799-09-5P 443799-10-8P 443799-12-0P
443799-14-2P 443799-16-4P 443799-18-6P 443799-20-0P 443799-22-2P
443799-24-4P 443799-25-5P 443799-26-6P 443799-27-7P 443799-28-8P
443799-29-9P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triazolediamine derivs. as kinase inhibitors)
IT 443799-53-9
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(preparation of triazolediamine derivs. as kinase inhibitors)
IT 443799-34-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, lithiation and carboxylation; preparation of triazolediamine derivs. as kinase inhibitors)
IT 364-83-0, 2',4'-Difluoroacetophenone

RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction to alc.; preparation of triazolediamine derivs. as kinase inhibitors)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Du Pont; GB 1065964 A 1967
(2) Gaetano, D; US 2352944 A 1944 HCAPLUS
(3) Glynn, S; WO 0109106 A 2001 HCAPLUS
(4) Green Cross Corp; EP 0710654 A 1996 HCAPLUS
(5) Song, C; WO 9921845 A 1999 HCAPLUS
IT **443798-55-8P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triazolediamine derivs. as kinase inhibitors)
RN 443798-55-8 HCAPLUS
CN 1H-1,2,4-Triazole-1-carbothioamide, 3-amino-5-[[4-(aminosulfonyl)phenyl]amino]-N-(2,6-difluorophenyl)- (9CI) (CA INDEX NAME)



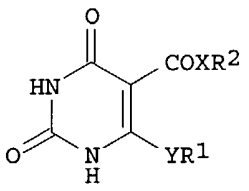
L108 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:881129 HCAPLUS
DN 134:42135
ED Entered STN: 15 Dec 2000
TI Preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases.
IN Salituro, Francesco; Bemis, Guy; Green, Jeremy; Fejzo, Jasna; Xie, Xiaoling
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-54
ICS C07D401-12; A61K031-505; C07D401-12; C07D239-00; C07D213-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000075118	A1	20001214	WO 2000-US15248	20000602 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003100549 A1 20030529 US 2001-8277 20011203 <--
PRAI US 1999-137523P P 19990603 <--
WO 2000-US15248 A1 20000602 <--
OS MARPAT 134:42135
GI



I

AB Title compds. [I; Y = O, NH, NR, S, SO, SO2; X = O, NH, NR; R1, R2 = H, (substituted) alkyl, alkenyl, (aromatic) (bicyclic) carbocyclyl, heterocyclyl; R = alkyl, alkenyl, (aromatic) (bicyclic) carbocyclyl, heterocyclyl], were prepared as inhibitors of c-JUN N-terminal kinases. Thus, I (R1Y, R2X = PhNH) inhibited JNK3 with IC50 <1 μM.

ST pyrimidinedione prepn jnk inhibitor; antiinflammatory pyrimidinedione; autoimmune disease treatment pyrimidinedione; bone disorder treatment pyrimidinedione; infectious disease treatment pyrimidinedione; neurodegenerative disease treatment pyrimidinedione; allergy inhibitor pyrimidinedione

IT Intestine, disease
(Crohn's, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Nervous system
(Huntington's chorea, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Sarcoma
(Kaposi's, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Respiratory distress syndrome
(adult, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Nervous system
(amyotrophic lateral sclerosis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Dermatitis
(atopic, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Heart, disease
(attack, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Stomach, disease
(autoimmune gastritis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

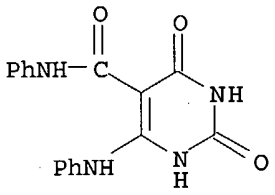
IT Nervous system
(degeneration, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)

IT Kidney, disease

(glomerulonephritis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Anemia (disease)
(hemolytic, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Heart, disease
(hypertrophy, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Intestine, disease
(inflammatory, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Reperfusion
(injury, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Brain, disease
(ischemia, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Antitumor agents
(leukemia; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT **Angiogenesis**
(**neovascularization**, treatment or ocular **neovascularization**; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Agranulocytosis
(neutropenia, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Pancreas, disease
(pancreatitis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Allergy inhibitors
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antiparkinsonian agents
Antitumor agents
Bone, disease
Platelet aggregation inhibitors
(preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Connective tissue
(scleroderma, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Brain, disease
(stroke, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Osteoporosis
(therapeutic agents; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Platelet (blood)
(thrombocytopenia, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Thyroid gland, disease
(thyroiditis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(treatment of disorders associated with proinflammatory cytokines; preparation

of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT **Angiogenesis**
Cell proliferation
(treatment of disorders; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Immunity
(treatment of pathol. immune response; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Hyperplasia
(treatment of vascular hyperplasia; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Autoimmune disease
Graves' disease
Hepatitis
Hypoxia, animal
Infection
Lupus erythematosus
Melanoma
Multiple myeloma
Multiple sclerosis
Myasthenia gravis
Psoriasis
(treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT Intestine, disease
(ulcerative colitis, treatment; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT 289898-51-7, c-JUN N-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT **264884-33-5 312752-09-3 312752-10-6**
312752-12-8 312752-13-9 312752-15-1
312752-17-3 312752-19-5 312752-21-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT 62-53-3, Aniline, reactions 108-59-8, Dimethyl malonate 10191-60-3, Dimethyl N-cyanodithioiminocarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
IT 136411-38-6P **312752-23-1P** 312752-24-2P 312752-25-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Allison; Immunopharmacology 2000, V47(2-3), P63 HCAPLUS
(2) Bell; J Heterocycl Chem 1983, V20(1), P41 HCAPLUS
(3) Bellon, S; WO 9958502 A 1999 HCAPLUS
(4) Bemis, G; WO 9964400 A 1999 HCAPLUS
(5) Brewer, A; US 4920126 A 1990 HCAPLUS
(6) Iordanov; Mol Cell Biol 1997, V17(6), P3373 HCAPLUS
(7) Lamon; Tetrahedron Lett 1970, 45, P3957 HCAPLUS
(8) Supko; J Liq Chromatogr 1991, V14(11), P2169 HCAPLUS
(9) Tominaga; J Heterocycl Chem 1991, V28(4), P1039 HCAPLUS
(10) Wang, Z; Structure 1998, V6(9), P1117 HCAPLUS
IT **264884-33-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of pyrimidinediones as inhibitors of c-JUN N-terminal kinases)
RN 264884-33-5 HCAPLUS
CN 5-Pyrimidinecarboxamide, 1,2,3,4-tetrahydro-2,4-dioxo-N-phenyl-6-(phenylamino)- (9CI) (CA INDEX NAME)



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L112 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:256049 HCAPLUS
DN 136:257237
ED Entered STN: 05 Apr 2002
TI Tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of the "classical" mitogen activated protein (MAP) kinase pathway
IN Dent, Paul; Grant, Steven; McKinstry, Robert; Dai, Yum
PA Virginia Commonwealth University, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-55
ICS A61K031-335; A01N043-02
CC 1-6 (**Pharmacology**)
Section cross-reference(s): 8
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002026236	A1	20020404	WO 2001-US30508	20010928 <--
WO 2002026236	C2	20030220		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-235938P P 20000928 <--
AB The present invention provides a method for treating cancer by promoting apoptosis and reducing clonogenic survival of cancer cells. The method encompasses co-administering 1) a cell cycle checkpoint abrogation agent (for example, UCN-01 or caffeine) and 2) an inhibitor of a compensatory cytoprotective pathway, such as an agent that inhibits the MEK 1/2 pathway (e.g.; PD98059, U0126, or PD184352) or an agent that inhibits the PI 3 pathway (e.g.; LY294002 or wortmanin). In addition, because the co-administration step also radiosensitizes cancer cells, the method addnl. encompasses the administration of radiation to further reduce clonogenic survival of cancer cells. The method promotes apoptosis and reduces clonogenic survival in many types of cancer cells, including leukemia cells, prostate cancer cells, breast cancer cells, myeloma cells,

and lymphoma cells.

ST antitumor cell cycle checkpoint abrogation MAP kinase; radiosensitizer tumor apoptosis MAP kinase

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-xL; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CREB (cAMP-responsive element-binding); tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(XIAP (X-linked inhibitor of apoptosis protein); tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(brain; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(carcinoma; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Intestine, neoplasm
(colon, inhibitors; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(colon; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Liver, neoplasm
(hepatoma, inhibitors; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(hepatoma; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Brain, neoplasm
(inhibitors; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(leukemia; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(lymphoma; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

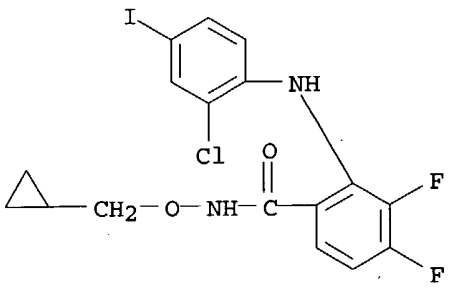
IT Antitumor agents
(mammary gland; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Mitochondria
(membrane potential; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Leukemia
(monocytic; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

IT Antitumor agents
(myeloma; tumor cell killing by cell cycle checkpoint abrogation

combined with inhibition of MAP kinase pathway)
IT Mammary gland
Prostate gland
(neoplasm, inhibitors; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p21CIP1; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p27KIP1; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT Antitumor agents
(prostate gland; tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT Antitumor agents
Apoptosis
Cell cycle
Cell proliferation
Radiosensitizers, biological
Radiotherapy
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT 9007-43-6, Cytochrome c, biological studies 115926-52-8, PI 3 kinase 137632-07-6, ERK1 protein kinase 137632-08-7, ERK2 protein kinase 140208-22-6, Cdc25C phosphatase 141436-78-4, Protein kinase C 142243-02-5, MAP kinase 142805-58-1, MEK-1 kinase 143375-65-9, Cdc2 kinase 150316-14-6, MEK2 kinase 155215-87-5, JNK kinase 165245-96-5, p38 Kinase 179241-78-2, Caspase 8 180189-96-2, Caspase 9 186322-81-6, Caspase 201556-11-8, Procaspase 3 201556-15-2, Procaspase 8 208778-60-3, Procaspase 9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT 112953-11-4, UCN-01 154447-36-6, LY 294002
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
IT 58-08-2, Caffeine, biological studies 19545-26-7, Wortmannin 109511-58-2, U 126 167869-21-8, PD 98059 **212631-79-3**, PD 184352 305350-87-2, SL 327
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Dai, Y; Cancer Res 2001, V61, P5106 HCAPLUS
(2) Daoud, S; US 6214821 B1 2001 HCAPLUS
(3) Deng; PNAS 2000, V97(4), P1578 HCAPLUS
(4) Dent; US 6147107 A 2000 HCAPLUS
(5) Sebolt-Leopold; Nat Med 1999, V5(7), P810 HCAPLUS
IT **212631-79-3**, PD 184352
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



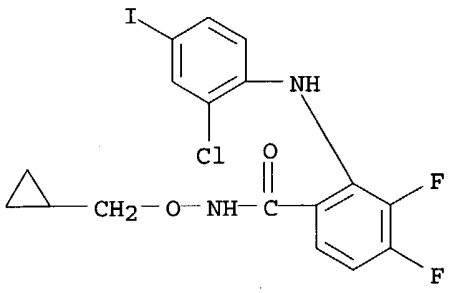
L112 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:171716 HCAPLUS
DN 136:210554
ED Entered STN: 08 Mar 2002
TI Inhibition of mitogen-activated protein kinase (MAPK) pathway as selective therapeutic strategy against melanoma
IN Vande Woude, George
PA Van Andel Institute, USA; Koo, Han-Mo
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC 1-6 (**Pharmacology**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002017952	A2	20020307	WO 2001-US27063	20010831 <--
	WO 2002017952	A3	20030424		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001088562	A5	20020313	AU 2001-88562	20010831 <--
	US 2002054869	A1	20020509	US 2001-942940	20010831 <--
	EP 1365796	A2	20031203	EP 2001-968307	20010831 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-229290P	P	20000901 <--		
	US 2001-285690P	P	20010424		
	WO 2001-US27063	W	20010831		

AB Inhibitors of the MAPK pathway, including MEK-directed proteases and small mol. inhibitors, are cytotoxic to human melanoma cells in vitro and in vivo via apoptotic mechanisms. These compds. are used to kill melanoma cells and to treat subjects with melanoma, either alone or in combination with other therapeutic modalities.
ST melanoma treatment MAPK inhibitor; mitogen activated protein kinase inhibitor melanoma treatment; MEK directed protease melanoma treatment
IT Proteins
RL: PAC (Pharmacological activity); BIOL (Biological study)
(Bacillus anthracis edema factor; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(LOX-IMVI; MAPK pathway inhibitors as selective therapeutic strategy

against melanoma)
IT Animal cell line
(M14; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(M19-MEL; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(MALME-3M; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Apoptosis
Cell cycle
Human
Signal transduction, biological
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Melanins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(SK-MEL-28; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(SK-MEL-2; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(SK-MEL-5; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(UACC-257; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Animal cell line
(UACC-62; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Toxins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anthrax lethal factor; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Toxins
RL: PAC (Pharmacological activity); BIOL (Biological study)
(anthrax protective antigen; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(central nervous system; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Nervous system
(central, neoplasm, inhibitors; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Intestine, neoplasm
(colon, inhibitors; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(colon; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Kidney, neoplasm
Ovary, neoplasm
(inhibitors; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(kidney; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)

IT Bacillus anthracis
(lethal factor; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(leukemia; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(lung non-small-cell carcinoma; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(mammary gland; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(melanoma; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Mammary gland
Prostate gland
(neoplasm, inhibitors; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Lung, neoplasm
(non-small-cell carcinoma, inhibitors; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(ovary; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Antitumor agents
(prostate gland; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT Drug interactions
(synergistic; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 142243-02-5, Mitogen-activated protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT 28822-58-4, IBMX
RL: PAC (Pharmacological activity); BIOL (Biological study)
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT 96251-59-1, DX-52-1 109511-58-2, U0126 167869-21-8, PD98059
212631-79-3, PD184352
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT 142805-58-1, MEK kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MEK-directed protease; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT 9001-92-7, Protease
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MEK-directed; MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
IT **212631-79-3**, PD184352
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(MAPK pathway inhibitors as selective therapeutic strategy against melanoma)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)

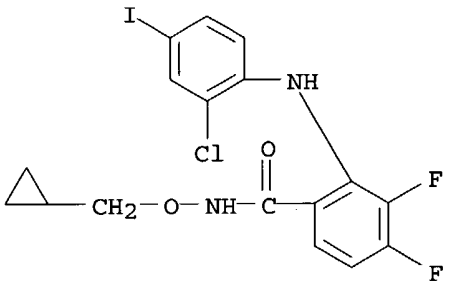


L112 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:747038 HCAPLUS
DN 135:283170
ED Entered STN: 12 Oct 2001
TI Use of MEK inhibitors for the production of medicaments against DNA and RNA viruses
IN Ludwig, Stephan; Pleschka, Stephan
PA Transmit Gesellschaft fuer Technologietransfer Mbh, Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61K031-352
CC 1-5 (**Pharmacology**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10017480	A1	20011011	DE 2000-10017480	20000407 <--
	WO 2001076570	A2	20011018	WO 2001-DE1292	20010405 <--
	WO 2001076570	A3	20020510		
	W: AU, CA, CN, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1274421	A2	20030115	EP 2001-935945	20010405 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	JP 2004505891	T2	20040226	JP 2001-574088	20010405 <--
	US 2003060469	A1	20030327	US 2002-240904	20021004 <--
PRAI	DE 2000-10017480	A	20000407 <--		
	WO 2001-DE1292	W	20010405		

AB The invention provides MEK inhibitors (e.g. U0126) for the production of medicaments for prophylaxis and antiviral therapy against DNA and RNA viruses, especially against intranuclear replicating neg. strand RNA viruses, e.g. influenza virus or Borna disease virus.
ST MEK inhibitor antiviral RNA DNA virus; U0126 antiviral RNA DNA virus; influenza virus antiviral MEK inhibitor; Borna disease virus antiviral MEK inhibitor
IT Antiviral agents
Borna disease virus
DNA viruses
Influenza A virus
Influenza virus
RNA viruses
(MEK inhibitors for production of medicaments against DNA and RNA viruses)
IT Drug delivery systems
(prodrugs; MEK inhibitors for production of medicaments against DNA and RNA viruses)
IT 109511-58-2 109511-58-2D, derivs. 167869-21-8 167869-21-8D, derivs.

212631-79-3 212631-79-3D, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(MEK inhibitors for production of medicaments against DNA and RNA viruses)
IT 142805-58-1, MEK kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MEK inhibitors for production of medicaments against DNA and RNA viruses)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 0042003 A1 HCAPLUS
(2) Anon; WO 0042029 A1 HCAPLUS
(3) Anon; WO 9837881 A1 HCAPLUS
(4) Chen, W; Experimental Lung Research 2000, V26, PS13
(5) Rodems, S; Journal Of Virology 1998, V72(11), PS9173
(6) Tang, P; Infection And Immunity 1998, V66(3), PS1106
IT **212631-79-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(MEK inhibitors for production of medicaments against DNA and RNA viruses)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:689470 HCAPLUS
DN 136:48126
ED Entered STN: 20 Sep 2001
TI Therapeutic targeting of the MEK/MAPK signal transduction module in acute myeloid leukemia
AU Milella, Michele; Kornblau, Steven M.; Estrov, Zeev; Carter, Bing Z.; Lapillonne, Helene; Harris, David; Konopleva, Marina; Zhao, Shourong; Estey, Elihu; Andreeff, Michael
CS Department of Blood and Marrow Transplantation, Section of Molecular Hematology and Therapy, The University of Texas, M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Journal of Clinical Investigation (**2001**), 108(6), 851-859
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal
LA English
CC 1-6 (**Pharmacology**)
AB The mitogen-activated protein kinase (MAPK) pathway regulates growth and survival of many cell types, and its constitutive activation has been implicated in the pathogenesis of a variety of malignancies. In this study we demonstrate that small-mol. MEK inhibitors (PD98059 and PD184352) profoundly impair cell growth and survival of acute myeloid leukemia (AML) cell lines and primary samples with constitutive MAPK activation. These

agents abrogate the clonogenicity of leukemic cells but have minimal effects on normal hematopoietic progenitors. MEK blockade also results in sensitization to spontaneous and drug-induced apoptosis. At a mol. level, these effects correlate with modulation of the expression of cyclin-dependent kinase inhibitors (p27Kip1 and p21Waf1/CIP1) and antiapoptotic proteins of the inhibitor of apoptosis proteins (IAP) and Bcl-2 families. Interruption of constitutive MEK/MAPK signaling therefore represents a promising therapeutic strategy in AML.

ST acute myeloid leukemia inhibitor PD98059 PD184352; MEK MAPK signal transduction antileukemia apoptosis

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IAP (inhibitor of apoptosis proteins); therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT Leukemia
(acute myelogenous, inhibitor; therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT Apoptosis
Hematopoietic precursor cell
Signal transduction, biological
(therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT 142805-58-1, Mek
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

IT 167869-21-8, PD98059 **212631-79-3**, PD184352
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

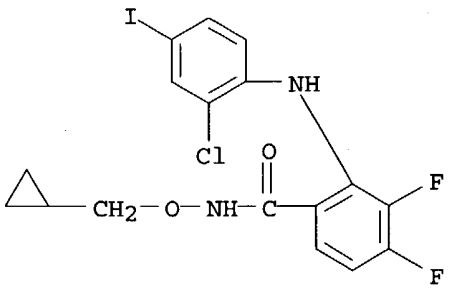
(1) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(2) Andreeff, M; Leukemia 1999, V13, P1881 HCAPLUS
(3) Blalock, W; Leukemia 2000, V14, P1080 HCAPLUS
(4) Blalock, W; Oncogene 2000, V19, P526 HCAPLUS
(5) Brognard, J; Cancer Res 2001, V61, P3986 HCAPLUS
(6) Carter, B; Blood 2001, V97, P2784 HCAPLUS
(7) Castilla, L; Nat Genet 1999, V23, P144 HCAPLUS
(8) Dash, A; Baillieres Best Pract Res Clin Haematol 2001, V14, P49 HCAPLUS
(9) Davies, S; Biochem J 2000, V351, P95 HCAPLUS
(10) Deng, X; Proc Natl Acad Sci 2000, V97, P1578 HCAPLUS
(11) Dent, P; Clin Cancer Res 2001, V7, P775 HCAPLUS
(12) Druker, B; Nat Med 1996, V2, P561 HCAPLUS
(13) Dudley, D; Proc Natl Acad Sci 1995, V92, P7686 HCAPLUS
(14) Erhardt, P; Mol Cell Biol 1999, V19, P5308 HCAPLUS
(15) Estrov, Z; Blood 1995, V86, P4594 HCAPLUS
(16) Fichelson, S; Blood 1999, V94, P1601 HCAPLUS
(17) Hayakawa, F; Oncogene 2000, V19, P624 HCAPLUS
(18) Hoshino, R; J Biol Chem 2000, V276, P2686
(19) Hunter, T; Cell 1997, V88, P333 HCAPLUS
(20) Jarpe, M; Oncogene 1998, V17, P1475 HCAPLUS
(21) Jarvis, W; Mol Pharmacol 1998, V54, P844 HCAPLUS

(22) Ketley, N; Blood 1997, V90, P4578 HCAPLUS
(23) Kim, S; Blood 1999, V93, P3893 HCAPLUS
(24) Lenferink, A; Proc Natl Acad Sci 2000, V97, P9609 HCAPLUS
(25) Lewis, T; Adv Cancer Res 1998, V74, P49 HCAPLUS
(26) Liu, Q; EMBO J 2000, V19, P1827 HCAPLUS
(27) Liu, Y; Cancer Res 1996, V56, P31 HCAPLUS
(28) Look, A; Science 1997, V278, P1059 HCAPLUS
(29) Lowenberg, B; N Engl J Med 1999, V341, P1051 MEDLINE
(30) Malumbres, M; Front Biosci 1998, V3, Pd887
(31) Morgan, M; Blood 2001, V97, P1823 HCAPLUS
(32) Rhoades, K; Blood 2000, V96, P2108 HCAPLUS
(33) Rosato, R; Int J Oncol 2001, V19, P181 HCAPLUS
(34) Sebolt-Leopold; Nat Med 1999, V5, P810 HCAPLUS
(35) Shayesteh, L; Nat Genet 1999, V21, P99 HCAPLUS
(36) Slingerland, J; J Cell Physiol 2000, V183, P10 HCAPLUS
(37) Towarari, M; Leukemia 1997, V11, P479
(38) Wang, Z; Cancer Res 1999, V59, P1259 HCAPLUS
(39) Xia, Z; Science 1995, V270, P1326 HCAPLUS
(40) Yang, H; J Biol Chem 2000, V275, P24735 HCAPLUS
(41) Yen, A; Cancer Res 1998, V58, P3163 HCAPLUS
(42) Yokozawa, T; Leukemid 2000, V14, P28 HCAPLUS
(43) Yu, C; Mol Pharmacol 2001, V60, P143 HCAPLUS
(44) Zhang, W; Clin Cancer Res 1995, V1, P1051 HCAPLUS

IT **212631-79-3**, PD184352
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic targeting of MEK/MAPK signal transduction module in acute myeloid leukemia)

RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:633080 HCAPLUS

DN 136:63675

ED Entered STN: 31 Aug 2001

TI MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of $\Delta\Psi m$ in HL-60 cells

AU Yu, Chunrong; Wang, Zhiliang; Dent, Paul; Grant, Steven

CS Department of Medicine, Virginia Commonwealth University, Richmond, VA, 23298, USA

SO Biochemical and Biophysical Research Communications (**2001**), 286(5), 1011-1018
CODEN: BBRCA9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

CC 1-6 (**Pharmacology**)

AB The effects of pharmacol. MEK1/2 inhibitors on ara-C-mediated mitochondrial injury, caspase activation, and apoptosis have been examined in HL-60 leukemic cells. Coadministration of subtoxic concns. of the MEK1/2 inhibitors U0126 (20 μM), PD98059 (40 μM), or PD184352 (10 μM) with 10-100 μM ara-C (6 h) potentiated apoptosis (i.e., by approx. twofold), and pro-caspase 3, pro-caspase 8, Bid, and PARP cleavage. Unexpectedly, MEK1/2 inhibitors failed to enhance ara-C-mediated loss of mitochondrial membrane potential (ΔΨm), but instead induced substantial increases in cytosolic release of cytochrome c and Smac/DIABLO. U0126/ara-C-mediated apoptosis and pro-caspase 3 activation, but not cytochrome c or Smac/DIABLO release, were blocked by the pan-caspase inhibitor ZVAD-fmk. Together, these findings indicate that potentiation of ara-C-mediated lethality in HL-60 cells by MEK1/2 inhibitors involves enhanced cytosolic release of cytochrome c and Smac/DIABLO but not discharge of ΔΨm, implicating activation of an apoptotic pathway that differs, at least with respect to the nature of the accompanying mitochondrial injury, from that triggered by ara-C alone. (c) 2001 Academic Press.

ST MEK1 inhibitor ara C leukemia apoptosis mechanism

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bid; pathway by which MEK1/2 inhibitors promote ara-C-induced apoptosis in HL-60 cells)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DIABLO; pathway by which MEK1/2 inhibitors promote ara-C-induced apoptosis in HL-60 cells)

IT Apoptosis
(MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT Membrane potential
(biol., mitochondrial; MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT Mitochondria
(injury; MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT Antitumor agents
(leukemia; MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT Mitochondria
(membrane, potential; MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT Membrane, biological
(mitochondrial, potential; MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT 142805-58-1, MEK-1 kinase 150316-14-6, MEK2 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT 147-94-4, Ara C 109511-58-2, U0126 167869-21-8, PD98059
212631-79-3, PD184352
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of ΔΨm in HL-60 cells)

IT 9055-67-8, Poly(ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cleavage; pathway by which MEK1/2 inhibitors promote ara-C-induced apoptosis in HL-60 cells)

IT 9007-43-6, Cytochrome c, biological studies 201556-11-8, Pro-caspase 3
201556-15-2, Pro-caspase 8
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(pathway by which MEK1/2 inhibitors promote ara-C-induced apoptosis in HL-60 cells)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

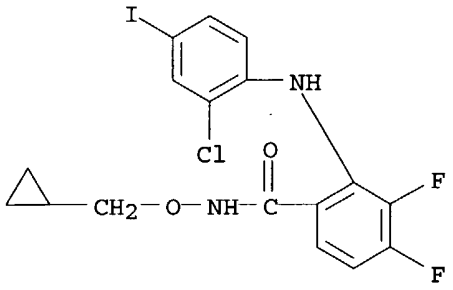
RE

(1) Achenbach, T; J Biol Chem 2000, V275, P32089 MEDLINE
(2) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(3) Backway, K; Cancer Res 1997, V57, P2446 HCAPLUS
(4) Boucher, M; J Cell Biochem 2000, V79, P355 HCAPLUS
(5) Chao, D; Annu Rev Immunol 1998, V16, P395 HCAPLUS
(6) Chauhan, D; J Biol Chem 1997, V272, P29995 HCAPLUS
(7) Chauhan, D; J Biol Chem 2001, V276, P24453 HCAPLUS
(8) Cross, T; Exp Cell Res 2000, V256, P34 HCAPLUS
(9) Deng, X; Proc Natl Acad Sci USA 2000, V97, P1578 HCAPLUS
(10) Early, A; Cancer Res 1982, V42, P1587 MEDLINE
(11) Favata, M; J Biol Chem 1998, V273, P18623 HCAPLUS
(12) Finucane, D; Exp Cell Res 1999, V251, P166 HCAPLUS
(13) Fulda, S; Oncogene 2001, V20, P1063 HCAPLUS
(14) Gross, A; J Biol Chem 1999, V274, P1156 HCAPLUS
(15) Hayakawa, J; Cancer Res 2000, V60, P5988 HCAPLUS
(16) Hengartner, M; Nature 2000, V407, P770 HCAPLUS
(17) Hoshino, R; J Biol Chem 2001, V276, P2686 HCAPLUS
(18) Jarvis, W; Mol Pharmacol 1998, V54, P844 HCAPLUS
(19) Jiang, X; J Biol Chem 2000, V275, P31199 HCAPLUS
(20) Kim, C; Cancer Res 1997, V57, P3115 HCAPLUS
(21) Kroemer, G; Nat Med 2000, V6, P513 HCAPLUS
(22) Li, X; Exp Cell Res 2000, V257, P290 HCAPLUS
(23) Mackeigan, J; J Biol Chem 2000, V275, P38953 HCAPLUS
(24) Matsuyama, S; J Biol Chem 1998, V273, P30995 HCAPLUS
(25) Pallis, M; Blood 2001, V98, P405 HCAPLUS
(26) Petit, P; FEBS Lett 1998, V426, P111 HCAPLUS
(27) Salvioli, S; FEBS Lett 1997, V411, P77 HCAPLUS
(28) Sebolt-Leopold, J; Nat Med 1999, V5(7), P810 HCAPLUS
(29) Slee, E; Cell Death Differ 1999, V6, P1067 HCAPLUS
(30) Srinivasula, S; Nature 2001, V410, P112 HCAPLUS
(31) Sun, X; J Biol Chem 1999, V274, P5053 HCAPLUS
(32) Susin, S; Biochem Biophys Acta 1998, V1366, P151 HCAPLUS
(33) Susin, S; J Exp Med 1997, V186, P25 HCAPLUS
(34) Tang, L; Biochem Pharmacol 2000, V60, P1445 HCAPLUS
(35) Tournier, C; Science 2000, V288, P870 HCAPLUS
(36) Tran, S; J Biol Chem 2001, V276, P16484 HCAPLUS
(37) Walczak, H; Exp Cell Res 2000, V256, P58 HCAPLUS
(38) Wang, Z; Cancer Res 1999, V59, P1259 HCAPLUS
(39) Xia, Z; Science 1995, V270, P1326 HCAPLUS
(40) Yang, J; Science 1997, V275, P1129 HCAPLUS
(41) Yu, C; Mol Pharmacol 2001, V60, P143 HCAPLUS
(42) Zamzami, N; Nat Rev Mol Cell Biol 2001, V2, P67 HCAPLUS
(43) Zamzami, N; Oncogene 1998, V16, P2265 HCAPLUS

IT **212631-79-3**, PD184352
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(MEK1/2 inhibitors promote ara-C-induced apoptosis but not loss of $\Delta\Psi m$ in HL-60 cells)

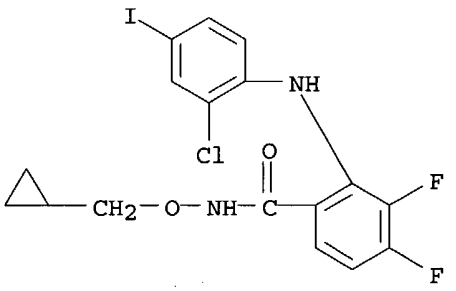
RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:563138 HCAPLUS
DN 135:353156
ED Entered STN: 03 Aug 2001
TI Effects of MAP kinase cascade inhibitors on the MKK5/ERK5 pathway
AU Mody, N.; Leitch, J.; Armstrong, C.; Dixon, J.; Cohen, P.
CS Medical Research Council Protein Phosphorylation Unit, School of Life Sciences, MSI/WTB Complex, University of Dundee, Dundee, DD1 5EH, UK
SO FEBS Letters (**2001**), 502(1,2), 21-24
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): **1**
AB Antibodies that recognize the active phosphorylated forms of mitogen-activated protein kinase (MAPK) kinase 5 (MKK5) and extracellular signal-regulated kinase 5 (ERK5) in untransfected cells have been exploited to show that the epidermal growth factor (EGF)-induced activation of MKK5 and ERK5 occurs subsequent to the activation of ERK1 and ERK2 in HeLa cells. The drugs U0126 and PD184352, which prevent the activation of MKK1 (and hence the activation of ERK1/ERK2), also prevent the activation of MKK5, although higher concns. are required. Our studies define physiol. targets of the MKK5/ERK5 pathway as proteins whose phosphorylation is largely prevented by 10 μM PD184352, but unaffected by 2 μM PD184352. Surprisingly, 2 μM PD184352 prolongs the activation of MKK5 and ERK5 induced by EGF or H2O2, indicating neg. control of the MKK5/ERK5 pathway by the classical MAPK cascade. Our results also indicate that ERK5 is not a significant activator of MAPK-activated protein kinase-1/RSK in HeLa cells.
ST MAP kinase cascade inhibitor MKK5 ERK5 pathway; EGF MKK5 ERK5 activation MAP kinase cascade inhibitor
IT Signal transduction, biological
(effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
IT Phosphorylation, biological
(protein; effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
IT 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(-induced activation of MKK5 and ERK5; effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
IT 90698-26-3 90698-26-3, RSK kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ERK5 is not a significant activator of MAPK-activated protein kinase-1/RSK in HeLa cells)
IT 137632-07-6, Protein kinase ERK1 137632-08-7, Protein kinase ERK2

170347-45-2, Protein kinase ERK5 327046-95-7, Mitogen-activated protein kinase kinase 5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
IT 109511-58-2, U0126 **212631-79-3**, PD184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Abe, J; J Biol Chem 1996, V271, P16586 HCAPLUS
(2) Alessi, D; EMBO J 1994, V13, P1610 HCAPLUS
(3) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(4) Alessi, D; Methods Enzymol 1995, V255, P279 HCAPLUS
(5) Anderson, N; Nature 1990, V343, P651 HCAPLUS
(6) Chao, T; J Biol Chem 1999, V274, P36035 HCAPLUS
(7) Davies, S; Biochem J 2000, V351, P95 HCAPLUS
(8) Dudley, D; Proc Natl Acad Sci 1995, V92, P7686 HCAPLUS
(9) English, J; J Biol Chem 1995, V270, P28897 HCAPLUS
(10) Fleming, Y; Biochem J 2000, V352, P145 HCAPLUS
(11) Kamakura, S; J Biol Chem 1999, V274, P26563 HCAPLUS
(12) Kato, Y; Nature 1998, V395, P713 HCAPLUS
(13) Pearson, G; J Biol Chem 2001, V276, P7927 HCAPLUS
(14) Sapkota, G; J Biol Chem 2001, V276, P19469 HCAPLUS
(15) Sebolt-Leopold, J; Nature Med 1999, V5, P810 HCAPLUS
(16) Sun, W; J Biol Chem 2001, V276, P5093 HCAPLUS
(17) Zhou, G; J Biol Chem 1995, V270, P12665 HCAPLUS
IT **212631-79-3**, PD184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of MAP kinase cascade inhibitors on MKK5/ERK5 pathway)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:503995 HCAPLUS
DN 135:298300
ED Entered STN: 12 Jul 2001
TI Pharmacological inhibitors of the mitogen-activated protein kinase (MAPK) kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells
AU Dai, Yun; Yu, Chunrong; Singh, Victor; Tang, Lin; Wang, Zhiliang; McInistry, Robert; Dent, Paul; Grant, Steven
CS Division of Hematology/Oncology, Medical College of Virginia, Richmond, VA, 23298, USA
SO Cancer Research (**2001**), 61(13), 5106-5115

CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 1-6 (**Pharmacology**)
AB Interactions between the checkpoint abrogator UCN-01 and several pharmacol. inhibitors of the mitogen-activated protein kinase (MAPK) kinase (MEK)/MAPK pathway have been examined in a variety of human leukemia cell lines. Exposure of U937 monocytic leukemia cells to a marginally toxic concentration of UCN-01 (e.g., 150 nM) for 18 h resulted in phosphorylation/activation of p42/44 MAPK. Coadministration of the MEK inhibitor PD184352 (10 μM) blocked UCN-01-induced MAPK activation and was accompanied by marked mitochondrial damage (e.g., cytochrome c release and loss of $\Delta\psi m$), caspase activation, DNA fragmentation, and apoptosis. Similar interactions were noted in the case of other MEK inhibitors (e.g., PD98059; U0126) as well as in multiple other leukemia cell types (e.g., HL-60, Jurkat, CCRF-CEM, and Raji). Coadministration of PD184352 and UCN-01 resulted in reduced binding of the cdc25C phosphatase to 14-3-3 proteins, enhanced dephosphorylation/activation of p34cdc2, and diminished phosphorylation of cAMP-responsive element binding protein. The ability of UCN-01, when combined with PD184352, to antagonize cdc25C/14-3-3 protein binding, promote dephosphorylation of p34cdc2, and potentiate apoptosis was mimicked by the ataxia telangiectasia mutation inhibitor caffeine. In contrast, cotreatment of cells with UCN-01 and PD184352 did not substantially increase c-Jun-NH2-terminal kinase activation nor did it alter expression of Bcl-2, Bcl-xL, Bax, or X-inhibitor of apoptosis. However, coexposure of U937 cells to UCN-01 and PD184352 induced a marked increase in p38 MAPK activation. Moreover, SB203580, which inhibits multiple kinases including p38 MAPK, partially antagonized cell death. Lastly, although UCN-01 ± PD184352 did not induce p21CIP1, stable expression of a p21CIP1 antisense construct significantly increased susceptibility to this drug combination. Together, these findings indicate that exposure of leukemic cells to UCN-01 leads to activation of the MAPK cascade and that interruption of this process by MEK inhibition triggers perturbations in several signaling and cell cycle regulatory pathways that culminate in mitochondrial injury, caspase activation, and apoptosis. They also raise the possibility that disrupting multiple signaling pathways, e.g., by combining UCN-01 with MEK inhibitors, may represent a novel antileukemic strategy.
ST MEK inhibitor UCN01 leukemia therapy signal transduction
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(14-3-3; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Bax; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Bcl-xL; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(CREB (cAMP-responsive element-binding); pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(XIAP; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bcl-2; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Antitumor agents
(leukemia; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Apoptosis
Cell cycle
Dephosphorylation, biological
Mitochondria
Signal transduction, biological
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Phosphorylation, biological
(protein; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT Drug interactions
(synergistic; pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT 186322-81-6, Caspase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

IT 109511-58-2, U0126 112953-11-4, UCN-01 152121-47-6, SB203580 167869-21-8, PD98059 **212631-79-3**, PD184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

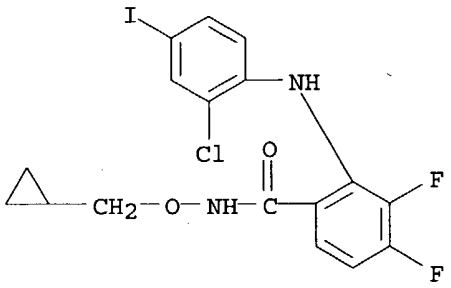
IT 137632-07-6, p44 Mitogen-activated protein kinase 137632-08-7, p42 Mitogen-activated protein kinase 140208-22-6, Cdc25C phosphatase 143375-65-9 155215-87-5 165245-96-5, p38 Mitogen-activated protein

kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)
IT 142243-02-5, Mitogen-activated protein kinase 142805-58-1, Mitogen-activated protein kinase kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Akinaga, S; Cancer Chemother Pharmacol 1993, V32, P183 HCAPLUS
(2) Akinaga, S; Cancer Chemother Pharmacol 1994, V33, P273 HCAPLUS
(3) Bertrand, R; Exp Cell Res 1994, V211, P314 HCAPLUS
(4) Blasina, A; Curr Biol 1999, V9, P1135 HCAPLUS
(5) Bonni, A; Science 1999, V286, P1358 HCAPLUS
(6) Bossy-Wetzel, E; EMBO J 1998, V17, P37 HCAPLUS
(7) Bunch, R; Clin Cancer Res 1996, V2, P791 HCAPLUS
(8) Cain, K; J Biol Chem 2000, V275, P6067 HCAPLUS
(9) Cardone, M; Science 1998, V282, P1318 HCAPLUS
(10) Chai, J; Nature 2000, V406, P855 HCAPLUS
(11) Chauhan, D; J Biol Chem 1997, V272, P29995 HCAPLUS
(12) Chen, X; Oncogene 1999, V18, P5691 HCAPLUS
(13) Chou, T; Adv Enzyme Regul 1984, V22, P27 HCAPLUS
(14) Cross, T; Exp Cell Res 2000, V256, P34 HCAPLUS
(15) Davies, S; Biochem J 2000, V351, P95 HCAPLUS
(16) Davis, S; J Neurosci 2000, V20, P4563 HCAPLUS
(17) Deng, X; Proc Natl Acad Sci 2000, V97, P1578 HCAPLUS
(18) Dudley, D; Proc Natl Acad Sci 1995, V92, P7686 HCAPLUS
(19) Favata, M; J Biol Chem 1998, V273, P18623 HCAPLUS
(20) Finucane, D; Exp Cell Res 1999, V251, P166 HCAPLUS
(21) Freemerman, A; Mol Pharmacol 1996, V49, P788 HCAPLUS
(22) Fuse, E; Cancer Res 1999, V59, P1054 HCAPLUS
(23) Ganiatsas, S; Proc Natl Acad Sci 1998, V95, P6881 HCAPLUS
(24) Gorczyca, W; Cancer Res 1993, V53, P1945 HCAPLUS
(25) Graves, P; J Biol Chem 2000, V275, P5600 HCAPLUS
(26) Haldar, S; Proc Natl Acad Sci 1995, V92, P4507 HCAPLUS
(27) Harkin, S; Mol Pharmacol 1998, V54, P663 HCAPLUS
(28) Harvey, S; Clin Cancer Res 2001, V7, P320 HCAPLUS
(29) Jarvis, W; Biochem Pharmacol 1994, V47, P839 HCAPLUS
(30) Jarvis, W; Cancer Res 1994, V54, P1707 HCAPLUS
(31) Jarvis, W; Mol Pharmacol 1998, V54, P844 HCAPLUS
(32) King, K; J Cell Biochem 1995, V58, P175 HCAPLUS
(33) Kitada, S; Blood 2000, V96, P393 HCAPLUS
(34) Kurata, N; Cancer Chemother Pharmacol 1999, V44, P12 HCAPLUS
(35) Lali, F; J Biol Chem 2000, V275, P7395 HCAPLUS
(36) Leppa, S; Oncogene 1999, V18, P6158 HCAPLUS
(37) Mizuno, K; FEBS Lett 1995, V359, P259 HCAPLUS
(38) Park, J; Mol Biol Cell 1999, V10, P4231 HCAPLUS
(39) Peng, C; Cell Growth Differ 1998, V9, P197 HCAPLUS
(40) Peng, C; Science 1997, V277, P1501 HCAPLUS
(41) Persons, D; J Biol Chem 2000, V275, P35778 HCAPLUS
(42) Pumiglia, K; Proc Natl Acad Sci 1997, V94, P448 HCAPLUS
(43) Riccio, A; Science 1999, V286, P2358 HCAPLUS
(44) Sebolt-Leopold, J; Nat Med 1999, V5, P810 HCAPLUS
(45) Segar, R; FASEB J 1995, V9, P726
(46) Shao, R; Cancer Res 1997, V57, P4029 HCAPLUS
(47) Shi, Z; Cancer Res 2001, V61, P1065 HCAPLUS

(48) Shimizu, T; Cancer Res 1995, V55, P228 HCAPLUS
(49) St Croix, B; Nat Med 1996, V2, P1204 MEDLINE
(50) Sun, X; J Biol Chem 1999, V274, P5053 HCAPLUS
(51) Suzuki, A; Mol Cell Biol 1999, V19, P3842 HCAPLUS
(52) Tang, L; Biochem Pharmacol 2000, V60, P1445 HCAPLUS
(53) Tibbles, L; Cell Mol Life Sci 1999, V55, P1230 HCAPLUS
(54) Tsuneoka, M; Oncogene 2000, V19, P115 HCAPLUS
(55) Verheij, M; Nature 1996, V380, P75 HCAPLUS
(56) Vrana, J; Blood 2001, V97, P2107
(57) Wang, Q; Cell Growth Differ 1995, V6, P927 HCAPLUS
(58) Wang, S; Mol Pharmacol 1997, V52, P1000 HCAPLUS
(59) Wang, Z; Cancer Res 1999, V59, P1259 HCAPLUS
(60) Wang, Z; Exp Cell Res 1998, V244, P105 HCAPLUS
(61) Wilson, W; Clin Cancer Res 2000, V6, P415 MEDLINE
(62) Xia, Z; Science 1995, V270, P1326 HCAPLUS
(63) Yang, J; Science 1997, V275, P1129 HCAPLUS
(64) Zhou, B; J Biol Chem 2000, V275, P10342 HCAPLUS

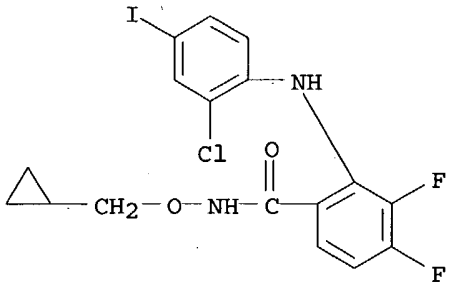
IT **212631-79-3**, PD184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacol. inhibitors of MAPK kinase/MAPK cascade interact synergistically with UCN-01 to induce mitochondrial dysfunction and apoptosis in human leukemia cells via perturbations in several signaling and cell cycle regulatory pathways)

RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:362914 HCAPLUS
DN 135:251181
ED Entered STN: 20 May 2001
TI Pharmacologic inhibitors of MKK1 and MKK2
AU Ahn, Natalie G.; Nahreini, Theresa Stines; Tolwinski, Nicholas S.; Resing, Katheryn A.
CS USA
SO Methods in Enzymology (**2001**), 332(Regulators and Effectors of Small GTPases, Part F), 417-431
CODEN: MENZAU; ISSN: 0076-6879
PB Academic Press
DT Journal; General Review
LA English
CC 1-0 (**Pharmacology**)
AB A review, with 26 refs., covers the inhibitor effects on activation and activity of mitogen-activated protein (MAP) kinase kinases 1 (MKK1) in vitro; inhibitor effects in intact cells; drug effects on extracellular signal-regulated kinases activation; mechanism of inhibitor action; and evaluation of inhibitor specificity. (c) 2001 Academic Press.

ST review MKK1 MKK2 inhibitor
IT 109511-58-2, U0126 167869-21-8, PD 98059 **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. inhibitors of MKK1 and MKK2)
IT 142243-02-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. inhibitors of MKK1 and MKK2)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(2) Alessi, D; Methods Enzymol 1995, V255, P279 HCAPLUS
(3) Boulton, T; Cell Regul 1991, V2, P357 HCAPLUS
(4) Cohen, P; Curr Opin Chem Biol 1999, V3, P459 HCAPLUS
(5) Dudley, D; Proc Natl Acad Sci USA 1995, V92, P7686 HCAPLUS
(6) Favata, M; J Biol Chem 1998, V273, P18623 HCAPLUS
(7) Frantz, B; Biochemistry 1998, V37, P13846 HCAPLUS
(8) Frost, J; EMBO J 1997, V16, P6426 HCAPLUS
(9) Giseli, D; Methods Enzymol (this volume) 2001, V332(Chap 26)
(10) Huang, C; Proc Natl Acad Sci USA 1996, V93, P10078 HCAPLUS
(11) Kamakura, S; J Biol Chem 1999, V274, P26563 HCAPLUS
(12) Lewis, T; Adv Cancer Res 1998, V74, P49 HCAPLUS
(13) Lewis, T; Molecular Cell, in press 2000
(14) Mansour, S; Biochemistry 1996, V35, P15529 HCAPLUS
(15) Melemed, A; Blood 1997, V90, P3462 HCAPLUS
(16) Moriguchi, T; J Biol Chem 1995, V270, P12969 HCAPLUS
(17) Reiners, J; Mol Pharmacol 1998, V53, P438 HCAPLUS
(18) Robbins, D; J Biol Chem 1993, V268, P5097 HCAPLUS
(19) Rojnuckarin, P; Blood 1999, V94, P1273 HCAPLUS
(20) Rouyez, M; Mol Cell Biol 1997, V17, P4991 HCAPLUS
(21) Schaeffer, H; Science 1998, V281, P1668 HCAPLUS
(22) Scheid, M; J Biol Chem 1996, V271, P18134 HCAPLUS
(23) Sebolt-Leopold, J; Nat Med 1999, V5, P810 HCAPLUS
(24) Shapiro, P; J Biol Chem 1998, V273, P1788 HCAPLUS
(25) Whalen, A; Mol Cell Biol 1997, V17, P1947 HCAPLUS
(26) Xu, S; Proc Natl Acad Sci USA 1995, V92, P6808 HCAPLUS
IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. inhibitors of MKK1 and MKK2)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:63820 HCAPLUS
DN 134:131318
ED Entered STN: 26 Jan 2001

TI Preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for the treatment of chronic pain

IN Bridges, Alexander James; Booth, Richard John; Tecle, Haile; Scaggs, Yvonne; Kaufman, Michael; Barrett, Stephen Douglas; Dixon, Alistair; Lee, Kevin; Pinnock, Robert Denham

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001005393	A2	20010125	WO 2000-US18348	20000705 <--
	WO 2001005393	A3	20010510		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1202724	A2	20020508	EP 2000-945140	20000705 <--
	EP 1202724	B1	20031001		
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	PT 1202724	T	20040227	PT 2000-945140	20000705 <--
	ZA 2001009909	A	20030228	ZA 2001-9909	20011130 <--
PRAI	US 1999-144280P	P	19990716 <--		
	US 1999-144320P	P	19990716 <--		
	US 1999-144419P	P	19990716 <--		
	US 1999-144655P	P	19990716 <--		
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OS MARPAT 134:131318

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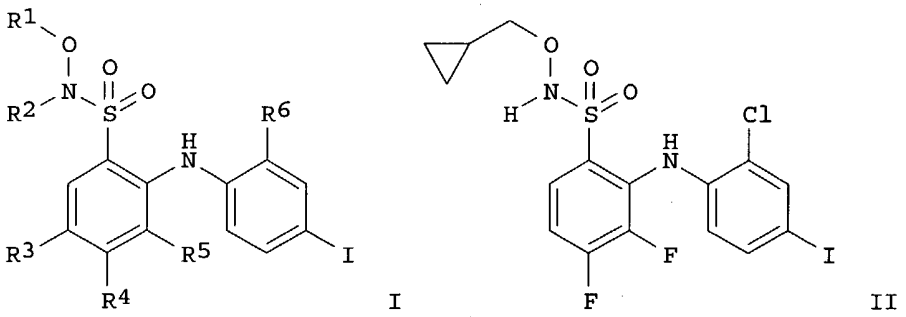

AB The title compds. (I) [wherein R1 = H, (phenyl)alkyl, (phenyl)alkenyl, (phenyl)alkynyl, cycloalkyl, Ph, cycloalkylalkyl, cycloalkylalkenyl, cycloalkylalkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, alkoxylalkyl, phenoxyalkyl, (un)substituted

aminoalkyl, piperidinoalkyl, morpholinoalkyl, or alkylpiperazinoalkyl; R2 = H, (cyclo)alkyl, Ph, heterocyclyl, or cycloalkylmethyl; R3 and R4 = independently H, F, NO2, Br, or Cl; R5 = H or F; R6 = H, F, Cl, or Me] were prepared for the treatment of chronic pain. For example, 2,3,4-trifluorobenzenesulfonyl chloride was amidated O-cyclopropylmethylhydroxylamine•HCl in CH2Cl2 using diisopropylethylamine (68%). Coupling with 2-chloro-4-iodoaniline in THF in the presence of Li bis(trimethylsilyl)amide afforded PD 297447 (II) in 73% yield. The APK IC50 for PD 297447 was 0.965 μM. Intrathecally administered II (30μg) showed no significant effect on allodynia in the CCI model of neuropathic pain in rats, perhaps due to low affinity or solubility of the compound However, related MEK inhibitors with higher affinities exerted an antiallodynic effect in CCI-induced neuropathic rats.

ST phenylamino benzamide benzenesulfonamide prepn mek inhibitor; sulfamoyl benzamide prepn analgesic; benzamide phenylamino sulfamoyl prepn chronic pain treatment

IT Pain
Skin, disease
(allodynia, treatment; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT Vitamins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(avitaminosis, treatment of pain associated with; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT Kidney, disease
(failure, treatment of pain associated with; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT Analgesics
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT Pain
(treatment of idiopathic and post-operative; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT Alcoholism
Arthritis
Hypothyroidism
Inflammation
(treatment of pain associated with; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 3463-30-7P, 1-(4-Nitrophenyl)-1H-pyrazole 4533-42-0P, 1-(4-Nitrophenyl)-1H-pyrrole 13788-94-8P, 3,5-Dimethyl-1-(4-nitrophenyl)-1H-pyrazole 17635-45-9P, 4-1H-Pyrazol-1-ylphenylamine 52708-32-4P, 4-(3,5-Dimethyl-1H-pyrazol-1-yl)benzenamine 52768-17-9P, 4-Pyrrol-1-ylphenylamine 197520-71-1P, 5-Nitro-2,3,4-trifluorobenzoic acid 283602-30-2P, 4-Fluoro-2-(4-methanesulfanylphenylamino)benzoic acid 283602-31-3P, 4-Fluoro-2-(4-methanesulfinylphenylamino)benzoic acid 283602-32-4P, 4-Fluoro-2-(4-methanesulfonylphenylamino)benzoic acid 283602-33-5P, 2-Methyl-4-trimethylsilanylethynylaniline 283602-34-6P 283602-35-7P, 4-Fluoro-2-(4-pyrrol-1-ylphenylamino)benzoic acid 283602-36-8P, 4-Fluoro-2-(4-pyrazol-1-ylphenylamino)benzoic acid 283602-37-9P, 2-[4-(3,5-Dimethylpyrazol-1-yl)phenylamino]-4-fluorobenzoic acid 283602-38-0P, N-Cyclopropylmethoxy-2,3,4-trifluorobenzenesulfonamide 285127-07-3P, 5-Dimethylsulfamoyl-2,3,4-trifluorobenzoic acid 285127-08-4P, 5-Dimethylsulfamoyl-2,3,4-trifluorobenzoic acid methyl ester 285127-09-5P, 1-Bis(4-methoxybenzyl)sulfamoyl-2,3,4-trifluorobenzene 285127-10-8P,

5-Bis(4-methoxybenzyl)sulfamoyl-2,3,4-trifluorobenzoic acid 285127-11-9P, 5-Bis(4-methoxybenzyl)sulfamoyl-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 285127-13-1P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-5-dimethylsulfamoylbenzoic acid 285127-14-2P, 3,4-Difluoro-5-dimethylsulfamoyl-2-(4-iodo-2-methylphenylamino)benzoic acid 321166-95-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 283602-00-6P, 4-Fluoro-2-(2-methyl-4-ethynylphenylamino)benzoic acid 285125-84-0P, 2-(2-Chloro-4-iodophenylamino)-5-dimethylsulfamoyl-3,4-difluorobenzoic acid methyl ester 285126-98-9P, 5-Bis(4-methoxybenzyl)sulfamoyl-2-(2-chloro-4-iodophenylamino)-3,4-difluorobenzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 219796-67-5P, 2,4-Bis(2-chloro-4-iodophenylamino)-3-fluoro-5-nitrobenzoic acid 283601-26-3P, 4-Fluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzoic acid 283601-27-4P, 5-Bromo-3,4-difluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzoic acid 283601-28-5P, 3,4-Difluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzoic acid 283601-29-6P, 2-(4-Methanesulfinyl-2-methylphenylamino)-4-nitrobenzoic acid 283601-30-9P, 3,4,5-Trifluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzoic acid 283601-31-0P, 3,4-Difluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzoic acid 283601-32-1P, 2-(2-Methyl-4-methylsulfanylphenylamino)-4-nitrobenzoic acid 283601-33-2P, 3,4,5-Trifluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzoic acid 283601-34-3P, 4-Fluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzoic acid 283601-35-4P, 5-Bromo-3,4-difluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzoic acid 283601-37-6P, 5-Bromo-3,4-difluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzoic acid 283601-38-7P, 3,4-Difluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzoic acid 283601-39-8P, 2-(4-Methanesulfonyl-2-methylphenylamino)-4-nitrobenzoic acid 283601-40-1P, N-Cyclopropylmethoxy-4-fluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-41-2P, 5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-42-3P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-43-4P, N-Cyclopropylmethoxy-2-(4-methanesulfinyl-2-methylphenylamino)-4-nitrobenzamide 283601-44-5P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-45-6P, N-Cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-46-7P, N-Cyclopropylmethoxy-2-(2-methyl-4-methylsulfanylphenylamino)-4-nitrobenzamide 283601-47-8P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-48-9P, N-Cyclopropylmethoxy-4-fluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-49-0P, 5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-50-3P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-51-4P, 5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-52-5P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-53-6P, N-Cyclopropylmethoxy-2-(4-methanesulfonyl-2-methylphenylamino)-4-nitrobenzamide 283601-54-7P,

4-Fluoro-N-hydroxy-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-55-8P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-56-9P, 3,4-Difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-57-0P, N-Hydroxy-2-(4-methanesulfinyl-2-methylphenylamino)-4-nitrobenzamide 283601-59-2P, 3,4,5-Trifluoro-N-hydroxy-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-60-5P, 3,4-Difluoro-N-hydroxy-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-61-6P, N-Hydroxy-2-(2-methyl-4-methylsulfanylphenylamino)-4-nitrobenzamide 283601-62-7P, 3,4,5-Trifluoro-N-hydroxy-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-63-8P, 4-Fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-64-9P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-65-0P, 3,4,5-Trifluoro-N-hydroxy-2-(2-methyl-4-methylsulfanylphenylamino)benzamide 283601-66-1P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methylphenylamino)benzamide 283601-67-2P, 3,4-Difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methylphenylamino)benzamide 283601-68-3P, N-Hydroxy-2-(4-methanesulfonyl-2-methylphenylamino)-4-nitrobenzamide 283601-69-4P, 3,4-Difluoro-2-(4-imidazol-1-yl-2-methylphenylamino)benzoic acid 283601-70-7P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-imidazol-1-yl-2-methylphenylamino)benzamide 283601-71-8P, 3,4-Difluoro-N-hydroxy-2-(4-imidazol-1-yl-2-methylphenylamino)benzamide 283601-72-9P, 3,4,5-Trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-ylphenylamino)benzoic acid 283601-73-0P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-ylphenylamino)benzamide 283601-74-1P, 3,4,5-Trifluoro-N-hydroxy-2-(2-methyl-4-[1,2,5]thiadiazol-3-ylphenylamino)benzamide 283601-75-2P, 2-[4-(4-Chloro-[1,2,5]thiadiazol-3-yl)-2-methylphenylamino]-3,4,5-trifluorobenzoic acid 283601-76-3P, 2-[4-(4-Chloro-[1,2,5]thiadiazol-3-yl)-2-methylphenylamino]-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 283601-77-4P, 2-[4-(4-Chloro-[1,2,5]thiadiazol-3-yl)-2-methylphenylamino]-3,4,5-trifluoro-N-hydroxybenzamide 283601-78-5P, 2-[4-[4-(2-Dimethylaminoethoxy)-[1,2,5]thiadiazol-3-yl]-2-methylphenylamino]-3,4,5-trifluorobenzoic acid 283601-79-6P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-[2-methyl-4-[4-(2-piperidin-1-ylethoxy)-[1,2,5]thiadiazol-3-yl]-phenylamino]benzamide 283601-80-9P, 3,4,5-Trifluoro-N-hydroxy-2-[2-methyl-4-[4-(2-morpholin-4-ylethoxy)-[1,2,5]thiadiazol-3-yl]phenylamino]benzamide 283601-81-0P, 5-Bromo-2-(2-chloro-4-methylsulfanylphenylamino)-3,4-difluorobenzoic acid 283601-82-1P, 2-(2-Chloro-4-methanesulfinylphenylamino)-3,4-difluorobenzoic acid 283601-83-2P, 2-(2-Chloro-4-methanesulfonylphenylamino)-3,4,5-trifluorobenzoic acid 283601-84-3P 283601-85-4P, 5-Bromo-2-(2-chloro-4-methanesulfonylphenylamino)-3,4-difluorobenzoic acid 283601-86-5P, 2-(2-Chloro-4-methanesulfonylphenylamino)-3,4-difluorobenzoic acid 283601-87-6P, 5-Bromo-2-(2-chloro-4-methylsulfanylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 283601-88-7P, 2-(2-Chloro-4-methanesulfinylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 283601-89-8P, 2-(2-Chloro-4-methanesulfonylphenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 283601-90-1P, 2-(2-Chloro-4-methylsulfanylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 283601-91-2P, 2-(2-Chloro-4-methanesulfinylphenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 283601-92-3P, 5-Bromo-2-(2-chloro-4-methanesulfonylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 283601-93-4P, 2-(2-Chloro-4-methylsulfanylphenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 283601-94-5P, 2-(2-Chloro-4-methanesulfonylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 283601-95-6P 283601-96-7P, 2-(2-Chloro-4-[1,2,5]thiadiazol-3-ylphenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 283601-97-8P 283601-98-9P 283601-99-0P 283602-01-7P, 5-Bromo-2-(4-ethynyl-2-methylphenylamino)-3,4-difluorobenzoic acid 283602-02-8P, N-Cyclopropylmethoxy-2-(4-ethynyl-2-

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2-methylphenylamino)benzenesulfonamide 284020-64-0P,
2-(4-Iodo-2-methylphenylamino)-4-nitrobenzenesulfonic acid 284020-65-1P,
N-Hydroxy-2-(4-iodo-2-methylphenylamino)-4-nitrobenzenesulfonamide
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fluorobenzenesulfonic acid 284020-68-4P, 2-(2-Chloro-4-iodophenylamino)-
4-fluoro-N-hydroxybenzenesulfonamide 284020-69-5P, 2-(2-Chloro-4-
iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzenesulfonamide
284020-70-8P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluorobenzenesulfonic
acid 284020-71-9P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-N-
hydroxybenzenesulfonamide 284020-72-0P, 2-(2-Chloro-4-iodophenylamino)-
3,4,5-trifluorobenzenesulfonic acid 284020-73-1P, 2-(2-Chloro-4-
iodophenylamino)-3,4,5-trifluoro-N-hydroxybenzenesulfonamide
284020-74-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-
trifluorobenzenesulfonamide 284020-75-3P, 5-Bromo-2-(2-chloro-4-
iodophenylamino)-3,4-difluorobenzenesulfonic acid 284020-76-4P,
5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-
hydroxybenzenesulfonamide 284020-77-5P, 5-Bromo-2-(2-chloro-4-
iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzenesulfonamide
284020-78-6P, 2-(2-Chloro-4-iodophenylamino)-4-nitrobenzenesulfonic acid
284020-79-7P, 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-
nitrobenzenesulfonamide 284020-80-0P, 2-(2-Chloro-4-iodophenylamino)-N-
cyclopropylmethoxy-4-nitrobenzenesulfonamide 285125-85-1P,
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-
sulfamoylbenzamide 285125-86-2P, 2-(2-Chloro-4-iodophenylamino)-3,4-
difluoro-N-hydroxy-5-sulfamoylbenzamide 285125-87-3P,
2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-5-sulfamoylbenzoic acid
285125-88-4P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-
difluoro-5-dimethylsulfamoylbenzamide 285125-89-5P, N-Cyclopropylmethoxy-
3,4-difluoro-5-dimethylsulfamoyl-2-(4-iodo-2-methylphenylamino)benzamide
285125-91-9P, 2-(2-Chloro-4-iodophenylamino)-4-sulfamoylbenzoic acid
285125-92-0P, 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-
sulfamoylbenzamide 285125-93-1P, 2-(2-Chloro-4-iodophenylamino)-N-
cyclopropylmethoxy-4-sulfamoylbenzamide 285125-94-2P,
2-(2-Chloro-4-iodophenylamino)-4-(2-morpholin-4-ylethylsulfamoyl)benzoic
acid 285125-95-3P, 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-(2-
morpholin-4-ylethylsulfamoyl)benzamide 285125-96-4P,
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-(2-morpholin-4-
ylethylsulfamoyl)benzamide 285125-97-5P, 2-(2-Chloro-4-iodophenylamino)-
3,4-difluoro-5-(2-morpholin-4-ylethylsulfamoyl)benzoic acid
285125-98-6P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-N-hydroxy-5-(2-
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iodophenylamino)benzamide 285126-02-5P 285126-03-6P,
N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodophenylamino)-5-[(pyridin-3-
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iodophenylamino)benzamide 285126-06-9P 285126-07-0P,
N-Cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxyethyl)pyridin-3-
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difluoro-2-(4-iodophenylamino)-5-(methylpyridin-2-
ylmethylsulfamoyl)benzamide 285126-11-6P, N-Cyclopropylmethoxy-3,4-
difluoro-2-(4-iodophenylamino)-5-[(pyridin-2-ylmethyl)sulfamoyl]benzamide

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methylphenylamino)-5-phenylsulfamoylbenzamide 285126-57-0P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-5-(pyridin-3-ylsulfamoyl)benzamide 285126-58-1P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxypropyl)pyridin-2-ylmethylsulfamoyl]benzamide 285126-59-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxyethyl)pyridin-2-ylmethylsulfamoyl]benzamide 285126-60-5P, 5-(Benzylpyridin-2-ylmethylsulfamoyl)-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 285126-61-6P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-4-ylmethyl)sulfamoyl]benzamide 285126-62-7P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-5-(ethylpyridin-4-ylmethylsulfamoyl)-3,4-difluorobenzamide 285126-63-8P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methylpyridin-4-ylmethylsulfamoyl)benzamide 285126-64-9P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxypropyl)pyridin-4-ylmethylsulfamoyl]benzamide 285126-65-0P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxyethyl)pyridin-4-ylmethylsulfamoyl]benzamide 285126-66-1P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methylphenylsulfamoyl)benzamide 285126-67-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-phenylsulfamoylbenzamide 285126-68-3P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(pyridin-3-ylsulfamoyl)benzamide 285126-99-0P, N-Allyloxy-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-5-(4-methylpiperazinesulfonyl)benzamide 285127-00-6P, N-Allyloxy-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-5-(methylphenylsulfamoyl)benzamide 285127-01-7P, 5-(Allylmethylsulfamoyl)-N-allyloxy-2-(2-chloro-4-iodophenylamino)-3,4-difluorobenzamide 285127-02-8P, 1-[5-Allyloxycarbamoyl-4-(2-chloro-4-iodophenylamino)-2,3-difluorobenzenesulfonyl]piperidine-3-carboxylic acid amide 285127-03-9P, N-Allyloxy-2-(2-chloro-4-iodophenylamino)-5-[(3-dimethylaminopropyl)methylsulfamoyl]-3,4-difluorobenzamide 285127-04-0P, N-Allyloxy-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-5-(4-pyridin-2-ylpiperazine-1-sulfonyl)benzamide 313676-66-3P, 2-(3',5'-Dichlorobiphenyl-4-ylamino)benzoic acid 321167-78-6P, 2-(2-Chloro-4-iodophenylamino)-3-fluoro-5-nitro-4-(3-sulfamoylphenylamino)benzoic acid 321167-81-1P, 2-(2-Chloro-4-iodophenylamino)-3-fluoro-5-nitro-4-(2-sulfamoylphenylamino)benzoic acid 321168-04-1P, 3,4,5-Trifluoro-2-(2-methyl-4-methylsulfanylphenylamino)benzoic acid 321171-65-7P, N-Cyclopropylmethoxy-2-(4-iodophenylamino)-4-phenylsulfamoylbenzamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 321171-68-0P, N-Cyclopropylmethoxy-2-(4-iodophenylamino)-4-(pyridin-3-ylsulfamoyl)benzamide 321171-71-5P, N-Cyclopropylmethoxy-2-(4-iodophenylamino)-4-[(pyridin-3-ylmethyl)sulfamoyl]benzamide 321171-74-8P, 4-(Bispyridin-3-ylmethylsulfamoyl)-N-cyclopropylmethoxy-2-(4-iodophenylamino)benzamide 321171-77-1P, N-Cyclopropylmethoxy-4-[(2-hydroxyethyl)pyridin-4-ylmethylsulfamoyl]-2-(4-iodophenylamino)benzamide 321171-80-6P, N-Cyclopropylmethoxy-2-(4-iodophenylamino)-4-(methylpyridin-3-ylmethylsulfamoyl)benzamide 321171-83-9P, N-Cyclopropylmethoxy-4-[(3-diethylaminopropyl)pyridin-3-ylmethylsulfamoyl]-2-(4-iodophenylamino)benzamide 321171-86-2P, N-Cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)-4-phenylsulfamoylbenzamide 321171-89-5P, N-Cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)-4-(pyridin-3-ylsulfamoyl)benzamide 321171-92-0P, N-Cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)-4-[(pyridin-3-ylmethyl)sulfamoyl]benzamide 321171-95-3P, 4-(Bispyridin-3-ylmethylsulfamoyl)-N-cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)benzamide 321171-98-6P, N-Cyclopropylmethoxy-4-

[(2-hydroxyethyl)pyridin-4-ylmethylsulfamoyl]-2-(4-iodo-2-methylphenylamino)benzamide 321172-01-4P, N-Cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)-4-(methylpyridin-3-ylmethylsulfamoyl)benzamide 321172-04-7P, N-Cyclopropylmethoxy-4-[(3-diethylaminopropyl)pyridin-3-ylmethylsulfamoyl]-2-(4-iodo-2-methylphenylamino)benzamide 321172-07-0P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-phenylsulfamoylbenzamide 321172-10-5P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-(pyridin-3-ylsulfamoyl)benzamide 321172-14-9P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-[(pyridin-3-ylmethyl)sulfamoyl]benzamide 321172-18-3P, 4-(Bispyridin-3-ylmethylsulfamoyl)-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxybenzamide 321172-21-8P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-[(2-hydroxyethyl)pyridin-4-ylmethylsulfamoyl]benzamide 321172-25-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-(methylpyridin-3-ylmethylsulfamoyl)benzamide 321172-29-6P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-[(3-diethylaminopropyl)pyridin-3-ylmethylsulfamoyl]benzamide 321172-45-6P 321858-06-4P, N-Allyloxy-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-5-(methoxymethylsulfamoyl)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 148553-50-8, Pregabalin 212631-61-3, PD 198306 **212631-79-3**, PD 184352 284030-47-3, PD 254552
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 142805-58-1, MEK kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT 100-01-6, 4-Nitroaniline, reactions 100-16-3, 4-Nitrophenylhydrazine 104-96-1 123-54-6, 2,4-Pentanedione, reactions 288-13-1, Pyrazole 350-46-9, 1-Fluoro-4-nitrobenzene 696-59-3, 2,5-Dimethoxytetrahydrofuran 1583-58-0, 2,4-Difluorobenzoic acid 17061-62-0, Bis-4-methoxybenzylamine 42016-93-3, 2-Chloro-4-iodoaniline 61079-72-9, 2,3,4-Trifluorobenzoic acid 74124-04-2, O-Cyclopropylmethylhydroxylamine hydrochloride 175278-08-7, 2,3,4-Trifluorobenzenesulfonyl chloride 285127-06-2, 1-Dimethylsulfamoyl-2,3,4-trifluorobenzene 321166-92-1, Lithium 5-bis(4-methoxybenzyl)sulfamoyl-2,3,4-trifluorobenzoate 321166-98-7, Lithium 2-chloro-4-iodoanilide 321167-01-5, Lithium 5-dimethylsulfamoyl-2,3,4-trifluorobenzoate
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of (phenylamino)benzenesulfonamides and (phenylamino)benzamides as MEK inhibitors for treatment of chronic pain)

RN 212631-79-3 HCAPLUS
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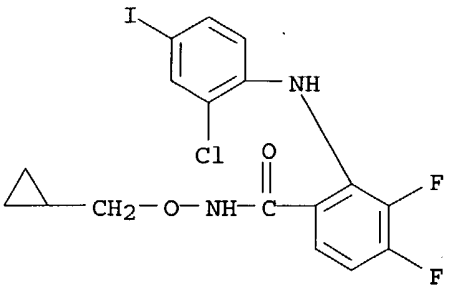

L112 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:63819 HCAPLUS
DN 134:131317
ED Entered STN: 26 Jan 2001
TI Preparation of 2-phenylaminobenzamides and analogs as MEK inhibitors for the treatment of chronic pain
IN Dixon, Alistair; Lee, Kevin; Pinnock, Robert Denham
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
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PI	WO 2001005392	A2	20010125	WO 2000-US18347	20000705 <--
	WO 2001005392	A3	20010719		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1202726	A2	20020508	EP 2000-943383	20000705 <--
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	WO 2000-US18347	W	20000705 <--		

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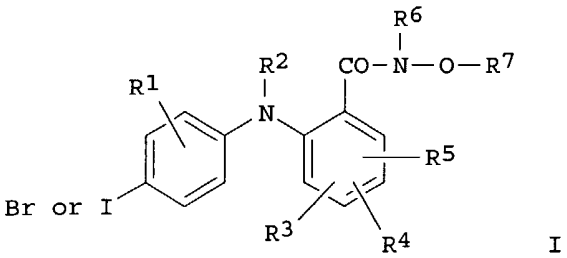

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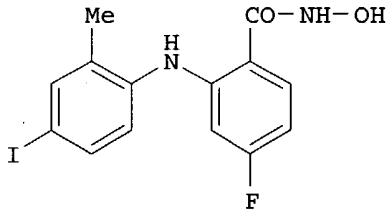


II

AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R2 = H; R3, R4, and R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m(CH2)nR9; R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = independently H, alkyl, or taken together with the N to which they are attached form a heterocycle; R6 = H, (cyclo)alkyl, acyl, aryl, or aralkyl; R7 = H, (cyclo)alkyl, alkenyl, alkynyl, or heterocyclyl] were prepared using conventional and combinatorial synthetic methods for the treatment of chronic pain. For example, 2,4-difluorobenzoic acid in THF was added to a solution of 2-amino-5-iodotoluene and Li diisopropylamide in THF/heptane/EtPh to give 4-fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid (47%). Treatment of the acid with O-(tetrahydro-2H-pyran-2-yl)hydroxylamine and diisopropylethylamine in THF/CH2Cl2 in the presence of PyBOP afforded the O-protected intermediate, which was dissolved in ethanolic HCl to give the title N-hydroxybenzamide (II) in 23% yield. Biol. assays indicated that MEK inhibitors exert an antiallodynic effect in CCI-induced neuropathic rats when administered intrathecally and that the antiallodynic effect correlates with the affinity of the compds.

ST phenylamino benzamide conventional combinatorial prepn mek inhibitor; benzamide prepn analgesic chronic pain treatment

IT Pain
Skin, disease
(allodynia, treatment; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT Vitamins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(avitaminosis, treatment of pain associated with; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT Kidney, disease
(failure, treatment of pain associated with; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT Analgesics
Combinatorial library
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK

inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT Pain
(treatment of idiopathic and post-operative; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT Alcoholism
Arthritis
Hypothyroidism
Inflammation
(treatment of pain associated with; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde 212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P, 5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P, 4-Fluoro-N-((tetrahydro-2H-pyran-2-yl)oxy)-2-(4-iodo-2-methylphenylamino)benzamide 212631-85-1P, 5-Bromo-2,3,4-trifluorobenzoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid 212631-86-2P, 5-Bromo-3,4-difluoro-N-((tetrahydro-2H-pyran-2-yl)oxy)-2-(4-iodo-2-methylphenylamino)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate 212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid 212628-52-9P, 4-Fluoro-2-(3-fluoro-4-iodo-2-methylphenylamino)benzoic acid 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid 212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid 212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid 212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid 212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid 212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P, 4-Fluoro-2-(2,3-dimethyl-4-iodophenylamino)benzoic acid 212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid 212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide

212628-78-9P, 4-Methoxy-N-(4-methoxyphenyl)-3-nitrobenzamide
212628-79-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide
212628-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide
212628-81-4P, N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide
212628-82-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide 212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-86-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)benzoylamino]acetic acid
212628-87-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide
212628-88-1P, 5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzyl alcohol 212628-96-1P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P, [2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P, 5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P, 3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P, 4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-12-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide
212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide
212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P, 2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-

ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide 212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methyl-phenylamino)benzamide 212629-56-6P, N-[2-[Bis(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methyl-phenylamino)benzamide 212629-60-2P, 5-Chloro-N-(3-diethylamino-2-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methyl-phenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-68-0P, N-[2-[Bis(2-hydroxyethyl)amino]ethyl]-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-69-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-71-5P, 5-Chloro-N-(3-diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-73-7P, 5-Chloro-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-75-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-77-1P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-piperidin-1-yl-ethyl)benzamide 212629-78-2P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperazin-1-ylethyl)benzamide 212629-79-3P, N-(2-Diethylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-80-6P, 5-Bromo-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-81-7P, N-(3-Hydroxypropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-82-8P, 5-Fluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-83-9P, N-(3-Diethylaminopropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-84-0P, N-(3-Diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-85-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-86-2P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(3-piperidin-1-yl-propyl)benzamide 212629-87-3P, 5-Bromo-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-

methylphenylamino)benzamide 212629-88-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-89-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-90-8P, N-(3-Diethylamino-2-hydroxypropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-91-9P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-92-0P, N-(3-Dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-93-1P, N-(2-Diisopropylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-94-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-95-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-98-6P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-benzyl ester 212629-99-7P, 5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-benzyl ester 212630-00-7P, N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-03-0P, 5-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212630-04-1P, N-Benzyloxy-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-05-2P, N-Benzyloxy-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-06-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(4-sulfamoylbenzyl)benzamide 212630-07-4P, N-(2-Hydroxyethyl)-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-08-5P, N-(2-Hydroxyethyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-09-6P, 2-(4-Iodo-2-methylphenylamino)-N-methyl-5-nitro-N-phenylbenzamide 212630-10-9P, 5-Chloro-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-11-0P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-12-1P, N-Allyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-13-2P, N-Benzyloxy-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-14-3P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-15-4P, N-Allyl-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212630-16-5P, N-Cyclopropyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-17-6P, 5-Bromo-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-18-7P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-19-8P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-20-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-21-2P, N-Allyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-22-3P, N-Allyl-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-23-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-24-5P, N-Cyclopropyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-25-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-26-7P, N-Benzyloxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-27-8P, N-Cyclohexyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-28-9P, N-Allyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P, [4-Chloro-2-(1H-tetrazol-5-yl)phenyl](4-iodo-2-methylphenyl)amine 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-40-5P, [4-Nitro-2-(1H-tetrazol-5-yl)phenyl](4-iodo-2-methylphenyl)amine 212630-41-6P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212630-42-7P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212630-43-8P, 2-(4-Bromo-2-

methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-methyl phenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(terahydro-2H-pyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(prop-2-ynyloxy)benzamide 212630-65-4P, 3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-ynyloxy)benzamide 212630-66-5P, 3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(1-methylprop-2-ynyloxy)benzamide 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methylprop-2-ynyloxy)benzamide 212630-68-7P, N-(But-3-ynyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-69-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-3-ynyloxy)-3,4-difluorobenzamide 212630-70-1P, 5-Bromo-N-(but-3-ynyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-71-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-phenylprop-2-ynyloxy)benzamide 212630-72-3P, 3,4-Difluoro-2-(4-bromo-2-methylphenylamino)-N-(3-phenylprop-2-ynyloxy)benzamide 212630-73-4P, 3,4-Difluoro-N-[3-(3-fluorophenyl)prop-2-ynyloxy]-2-(4-iodo-2-methylphenylamino)benzamide 212630-74-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-[3-(3-fluorophenyl)prop-2-ynyloxy]benzamide 212630-75-6P, 3,4-Difluoro-N-[3-(2-fluorophenyl)prop-2-ynyloxy]-2-(4-iodo-2-methylphenylamino)benzamide 212630-76-7P, 5-Bromo-3,4-difluoro-N-[3-(2-fluorophenyl)-prop-2-ynyloxy]-2-(4-iodo-2-methylphenylamino)benzamide 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide 212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P, 4-Fluoro-2-(4-iodo-2-methylphenylam ino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-91-6P, N-Cyclopropylmethoxy-3,4-

difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-94-9P, 5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-methylallyloxy)benzamide 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide 212631-09-9P, 2-(4-Bromo-2-methylphenylamino)-N-(4,4-dimethyl-2-pentynyloxy)-3,4-difluorobenzamide 212631-13-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(prop-2-enyloxy)benzamide 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P, 5-Bromo-N-butoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-29-3P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbut-2-enyloxy)benzamide 212631-30-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylpent-2-en-4-ynyloxy)benzamide 212631-32-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(prop-2-ynyloxy)benzamide 212631-33-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-[3-(3-methoxyphenyl)prop-2-ynyloxy]benzamide 212631-34-0P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-35-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(pyridin-3-ylmethoxy)benzamide 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P, 4-Bromo-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212631-38-4P, 5-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-39-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212631-40-8P, 3,4,5-Trifluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-41-9P, 5-Chloro-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-42-0P, 5-Bromo-3,4-difluoro-2-(2-fluoro-4-iodophenylamino)-N-hydroxybenzamide 212631-43-1P, N-Hydroxy-2-(4-iodo-2-methylphenylamino)-4-nitrobenzamide 212631-44-2P, 3,4,5-Trifluoro-2-(2-fluoro-4-iodophenylamino)-N-hydroxybenzamide 212631-45-3P, 5-Chloro-3,4-difluoro-2-(2-fluoro-4-iodophenylamino)-N-hydroxybenzamide 212631-46-4P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-47-5P, 2-(2-Fluoro-4-iodophenylamino)-N-hydroxy-4-nitrobenzamide 212631-48-6P, 2-(2-Chloro-4-iodophenylamino)-3,4,5-trifluoro-N-hydroxybenzamide 212631-49-7P, 5-Chloro-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-50-0P, 5-Bromo-2-(2-bromo-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-51-1P, 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-methylbenzamide 212631-52-2P, 2-(2-Bromo-4-iodophenylamino)-3,4,5-trifluoro-N-hydroxybenzamide 212631-54-4P, 2-(2-Bromo-4-iodophenylamino)-N-hydroxy-4-nitrobenzamide 212631-55-5P, 4-Fluoro-2-(2-fluoro-4-iodophenylamino)-N-hydroxybenzamide 212631-56-6P,

3,4-Difluoro-2-(2-fluoro-4-iodophenylamino)-N-hydroxybenzamide 212631-57-7P, 2-(2-Chloro-4-iodophenylamino)-4-fluoro-N-hydroxybenzamide 212631-58-8P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-59-9P, 2-(2-Bromo-4-iodophenylamino)-4-fluoro-N-hydroxybenzamide 212631-60-2P, 2-(2-Bromo-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-61-3P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-62-4P, 5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-63-5P, 5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzamide 212631-64-6P, N-Cyclopropylmethoxy-2-(4-iodo-2-methylphenylamino)-4-nitrobenzamide 212631-65-7P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(2-fluoro-4-iodophenylamino)benzamide 212631-66-8P, 5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzamide 212631-67-9P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212631-68-0P, N-Cyclopropylmethoxy-2-(2-fluoro-4-iodophenylamino)-4-nitrobenzamide 212631-69-1P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 212631-70-4P, 5-Chloro-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212631-71-5P, 5-Bromo-2-(2-bromo-4-iodophenylamino)-N-ethoxy-3,4-difluorobenzamide 212631-72-6P, 2-(2-Chloro-4-iodophenylamino)-N-ethoxy-4-nitrobenzamide 212631-73-7P, 2-(2-Bromo-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide 212631-75-9P, 2-(2-Bromo-4-iodophenylamino)-N-cyclopropylmethoxy-4-nitrobenzamide 212631-76-0P, N-Cyclopropylmethoxy-4-fluoro-2-(2-fluoro-4-iodophenylamino)benzamide 212631-77-1P, N-Cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzamide 212631-78-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide **212631-79-3P**, 3,4-Difluoro-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxybenzamide 212631-80-6P, 2-(2-Bromo-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide 212631-81-7P, 2-(2-Bromo-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-48-7P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-isopropylbenzamide 219777-50-1P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 219777-52-3P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 219777-54-5P, 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-nitrobenzamide 219777-58-9P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 219777-60-3P, 3,4-Difluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 219777-61-4P, 3,4-Difluoro-5-bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethoxy)benzamide 219777-92-1P, 2-(2-Chloro-4-iodophenylamino)-4-fluoro-N-hydroxybenzamide hydrochloride salt 219777-97-6P, 2-(2-Chloro-4-iodophenylamino)-4-fluoro-N-(tetrahydropyran-2-yloxy)benzamide 219778-04-8P, 3,4-Difluoro-2-(2-chloro-4-iodophenylamino)-N-cyclobutylmethoxybenzamide 219778-06-0P, 3,4-Difluoro-2-(2-chloro-4-iodophenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 219778-09-3P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-N-(2-dimethylaminoethoxy)-3,4-difluorobenzamide monohydrochloride salt 219778-12-8P, 5-Bromo-N-(2-dimethylaminopropoxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 219778-19-5P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-(tetrahydropyran-2-yloxy)benzamide 219778-24-2P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethoxy)benzamide 219778-35-5P, 5-Bromo-N-(2-diethylaminoethoxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 219778-40-2P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isobutoxybenzamide 219778-43-5P, 5-Bromo-N-cyclohexylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 219778-48-0P, 5-Bromo-N-cyclopentylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 219778-52-6P, 5-Bromo-N-cyclobutylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 219794-13-5P, 5-Bromo-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-benzyl ester

219794-21-5P, 2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester 219796-61-9P, 2-(2-Chloro-4-iodophenylamino)-3-fluoro-4-(2-morpholin-4-ylethylamino)-5-nitrobenzoic acid 219796-66-4P, 4-Amino-2-(2-chloro-4-iodophenylamino)-3-fluoro-5-nitrobenzoic acid 219796-67-5P, 2,4-Bis(2-chloro-4-iodophenylamino)-3-fluoro-5-nitrobenzoic acid 219796-68-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrobenzoic acid 219796-71-1P, 2-(2,6-Difluoro-4-iodophenylamino)-3,4-difluorobenzoic acid 219796-73-3P, 2-(2-Chloro-4-iodophenylamino)-4-nitrobenzoic acid 219796-74-4P, 2-(2,4-Diiodophenylamino)-4-fluorobenzoic acid 219796-75-5P, 2-(2-Bromo-4-iodophenylamino)-4-fluorobenzoic acid 219796-76-6P, 4-Fluoro-2-(2-fluoro-4-iodophenylamino)benzoic acid 219796-77-7P, 2-(2-Chloro-4-iodophenylamino)-4-fluorobenzoic acid 219796-79-9P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluorobenzoic acid 219800-81-4P, 2,3,5-Trifluoro-6-(4-iodo-2-methylphenylamino)-4-(4-methylpiperazin-1-yl)benzoic acid methyl ester dihydrofluoride salt 219800-86-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid N',N'-dimethylhydrazide 219800-90-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid hydrazide 219802-06-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(4-methylpiperazin-1-yl)benzamide 277335-40-7P, 5-Bromo-2-(4-iodo-2-ethylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 277335-43-0P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylbenzyl)-N-[5-(3-methoxyphenyl)-3-methylpent-2-en-4-ynyloxy]benzamide 278610-42-7P, 5-Chloro-2-(2-chloro-4-iodophenylamino)-3,4-difluorobenzoic acid 278610-51-8P, 5-Chloro-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 284030-47-3P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)1H-benzimidazole-5-carboxylic acid cyclopropylmethoxyamide 303175-44-2P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluorobenzoic acid 321438-66-8P, N-(2-Hydroxyethyl)-2-(4-iodo-2-ethylphenylamino)-5-nitrobenzamide 321438-67-9P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)benzamide potassium salt 321438-68-0P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 321438-69-1P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide hydrochloride salt 321438-70-4P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-N-(2-hydroxyethoxy)benzamide 321438-71-5P, 3,4-Difluoro-N-(2-hydroxyethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 321438-72-6P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-(3-hydroxypropoxy)benzamide 321438-73-7P, 2-(2-Chloro-4-iodophenylamino)-3,4,5-trifluoro-N-(3-hydroxypropoxy)benzamide 321438-74-8P, 2-(2-Chloro-4-iodophenylamino)-3,4,5-trifluoro-N-[2-(2-methoxyethoxy)ethoxy]benzamide 321438-75-9P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-N-(3-hydroxypropoxy)benzamide 321438-76-0P, 5-Bromo-3,4-difluoro-N-(3-hydroxypropoxy)-2-(4-iodo-2-methylphenylamino)benzamide 321438-77-1P, 3,4,5-Trifluoro-N-(3-hydroxypropoxy)-2-(4-iodo-2-methylphenylamino)benzamide 321438-78-2P, 3,4,5-Trifluoro-N-(2-hydroxyethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 321438-79-3P, 2-(2-Chloro-4-iodophenylamino)-3,4-difluoro-5-nitrobenzoic acid 321438-80-6P, 2-(2-Chloro-4-iodophenylamino)-3,4,5-trifluorobenzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 148553-50-8, Pregabalin 283602-39-1 285125-85-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 142805-58-1, MEK kinase

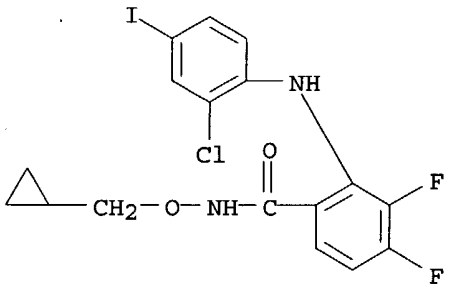
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)hydroxylamine 13194-68-8, 2-Amino-5-iodotoluene 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

IT **212631-79-3P**, 3,4-Difluoro-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxybenzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-phenylaminobenzamide and 2-phenylaminobenzoic acid MEK inhibitors by conventional and combinatorial synthetic methods for treatment of chronic pain)

RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:63818 HCAPLUS

DN 134:131540

ED Entered STN: 26 Jan 2001

TI Preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for the treatment of chronic pain

IN Barrett, Stephen Douglas; Bridges, Alexander James; Tecle, Haile; Dixon, Alistair; Lee, Kevin; Pinnock, Robert Denham; Zhang, Lu-Yan

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2001005391	A2	20010125	WO 2000-US18346	20000705	<--
	WO 2001005391	A3	20010719			

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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WO 2000-US18346 W 20000705 <--
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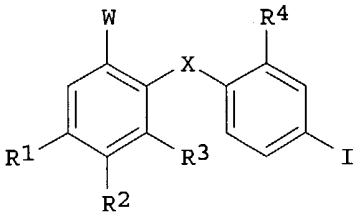

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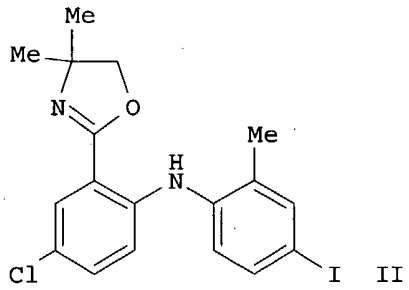

II

AB The title compds. (I) [wherein W = a variety of (un)substituted heterocycles; X = NRF; RF = H or (un)substituted alkyl; R1 and R2 = independently H, F, NO2, Br, Cl, or taken together with the benzene ring to which they are attached form an (un)substituted (iso)indole, benzofuran, benzothiophene, indazole, benzimidazole, or benzthiazole ring; or R1 = SO2NRGRH; R3 H or F; RG, RH, and R4 = independently H, Cl, or Me; R5 = H or (un)substituted alkyl] were prepared for the treatment of chronic pain. For example, cycloaddn. of 2-amino-2-methyl-1-propanol with 5-chloro-2-methoxybenzoic acid using SOCl2 in CH2Cl2 gave 2-(5-chloro-2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (77%). Treatment with 4-iodo-2-methylaniline in THF in the presence of LDA afforded the diphenylamine (II) in 77% yield. Biol. assays indicated that MEK inhibitors exert an antiallodynic effect in CCI-induced neuropathic rats when administered intrathecally, and that the antiallodynic effect correlates with the affinity of the compds.

ST heterocyclylphenyl iodophenyl amine prepn mek inhibitor; phenylamine prepn analgesic; iodophenyl heterocyclylphenyl amine prepn chronic pain treatment

IT Pain
Skin, disease
(allodynia, treatment; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT Vitamins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(avitaminosis, treatment of pain associated with; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT Kidney, disease
(failure, treatment of pain associated with; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT Analgesics
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors

for treatment of chronic pain)

IT Pain
(treatment of idiopathic and post-operative; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT Alcoholism
Arthritis
Hypothyroidism
Inflammation
(treatment of pain associated with; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 82400-14-4P, 2-(5-Chloro-2-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 284032-14-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid methyl ester 284032-17-3P, 2-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoyl]hydrazinecarbothioamide 284033-41-6P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid hydrazide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 219796-67-5P, 2,4-Bis(2-chloro-4-iodophenylamino)-3-fluoro-5-nitrobenzoic acid 284032-11-7P, [4-Chloro-2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenyl]-(4-iodo-2-methylphenyl)amine hydrochloride salt 284032-12-8P, [2,3-Difluoro-6-(1H-tetrazol-5-yl)phenyl]-(4-iodo-2-methylphenyl)amine 284032-13-9P, [6-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-2,3-difluorophenyl]-(4-iodo-2-methylphenyl)amine 284032-15-1P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ylamine 284032-16-2P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl][1,3,4]oxadiazol-2-ylamine 284032-18-4P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazole-3-thiol 284032-19-5P, (2,3-Difluoro-6-[1,3,4]oxadiazol-2-ylphenyl)-(4-iodo-2-methylphenyl)amine 284032-20-8P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazole-2-thiol 284032-21-9P, [5-Fluoro-2-(1H-tetrazol-5-yl)phenyl]-(4-iodo-2-methylphenyl)amine 284032-22-0P, (4-Iodo-2-methylphenyl)-[2,3,4-trifluoro-6-(1H-tetrazol-5-yl)phenyl]amine 284032-23-1P, [4-Bromo-2,3-difluoro-6-(1H-tetrazol-5-yl)phenyl]-(4-iodo-2-methylphenyl)amine 284032-24-2P, [5-Fluoro-4-nitro-2-(1H-tetrazol-5-yl)phenyl]-(4-iodo-2-methylphenyl)amine 284032-25-3P, [2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-fluorophenyl]-(4-iodo-2-methylphenyl)amine 284032-26-4P, [6-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-2,3,4-trifluorophenyl]-(4-iodo-2-methylphenyl)amine 284032-27-5P, [4-Bromo-6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2,3-difluorophenyl]-(4-iodo-2-methylphenyl)amine 284032-28-6P, [2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-fluoro-4-nitrophenyl]-(4-iodo-2-methylphenyl)amine 284032-29-7P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ol 284032-30-0P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ol 284032-31-1P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ol 284032-32-2P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ol 284032-33-3P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]thiadiazol-2-ol 284032-34-4P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ol 284032-35-5P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ol 284032-36-6P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ol 284032-37-7P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-

[1,3,4]oxadiazol-2-ol 284032-38-8P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]oxadiazol-2-ol 284032-39-9P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ol 284032-40-2P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ol 284032-41-3P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ol 284032-42-4P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ol 284032-43-5P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-4H-[1,2,4]triazol-3-ol 284032-44-6P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ylamine 284032-45-7P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ylamine 284032-46-8P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ylamine 284032-47-9P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazol-2-ylamine 284032-48-0P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]thiadiazol-2-ylamine 284032-49-1P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ylamine 284032-50-4P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ylamine 284032-51-5P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazol-2-ylamine 284032-52-6P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]oxadiazol-2-ylamine 284032-53-7P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ylamine 284032-54-8P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ylamine 284032-55-9P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazol-3-ylamine 284032-56-0P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-4H-[1,2,4]triazol-3-ylamine 284032-57-1P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazole-2-thiol 284032-58-2P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazole-2-thiol 284032-59-3P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazole-2-thiol 284032-60-6P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]thiadiazole-2-thiol 284032-61-7P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]thiadiazole-2-thiol 284032-62-8P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazole-2-thiol 284032-63-9P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazole-2-thiol 284032-64-0P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-[1,3,4]oxadiazole-2-thiol 284032-65-1P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-[1,3,4]oxadiazole-2-thiol 284032-66-2P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazole-3-thiol 284032-67-3P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazole-3-thiol 284032-68-4P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4H-[1,2,4]triazole-3-thiol 284032-69-5P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-4H-[1,2,4]triazole-3-thiol 284032-70-8P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-71-9P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-72-0P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-73-1P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-74-2P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]isothiazol-3-ol 284032-75-3P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-76-4P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-77-5P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-78-6P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-79-7P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]isoxazol-3-ol 284032-80-0P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-pyrazol-

3-ol 284032-81-1P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-pyrazol-3-ol 284032-82-2P, 5-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-pyrazol-3-ol 284032-83-3P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-pyrazol-3-ol 284032-84-4P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-1H-pyrazol-3-ol 284032-85-5P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-86-6P, 4-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-87-7P, 4-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-88-8P, 4-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isothiazol-3-ol 284032-89-9P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]isothiazol-3-ol 284032-90-2P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-91-3P, 4-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-92-4P, 4-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-93-5P, 4-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]isoxazol-3-ol 284032-94-6P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]isoxazol-3-ol 284032-95-7P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1-methyl-1H-pyrazol-3-ol 284032-96-8P, 4-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1-methyl-1H-pyrazol-3-ol 284032-97-9P, 1-Methyl-4-[3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-pyrazol-3-ol 284032-98-0P, 4-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1-methyl-1H-pyrazol-3-ol 284032-99-1P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-1-methyl-1H-pyrazol-3-ol 284033-00-7P, 5-[2-(2-Amino-4-iodophenylamino)-4-fluorophenyl]-1-methyl-1H-[1,2,3]triazol-4-ol 284033-01-8P, 5-[2-(2-Amino-4-iodophenylamino)-3,4-difluorophenyl]-1-methyl-1H-[1,2,3]triazol-4-ol 284033-02-9P, 5-[2-(2-Amino-4-iodophenylamino)-3,4,5-trifluorophenyl]-1-methyl-1H-[1,2,3]triazol-4-ol 284033-03-0P, 5-[2-(2-Amino-4-iodophenylamino)-5-bromo-3,4-difluorophenyl]-1-methyl-1H-[1,2,3]triazol-4-ol 284033-04-1P, 5-[2-(2-Amino-4-iodophenylamino)-4-fluoro-5-nitrophenyl]-1-methyl-1H-[1,2,3]triazol-4-ol 284033-05-2P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-3-methyl-3H-[1,2,3]triazol-4-ol 284033-06-3P, 5-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-3-methyl-3H-[1,2,3]triazol-4-ol 284033-07-4P, 3-Methyl-5-[3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-3H-[1,2,3]triazol-4-ol 284033-08-5P, 5-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-3-methyl-3H-[1,2,3]triazol-4-ol 284033-09-6P, 5-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-3-methyl-3H-[1,2,3]triazol-4-ol 284033-10-9P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2-methyl-2H-pyrazol-3-ol 284033-11-0P, 4-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2-methyl-2H-pyrazol-3-ol 284033-12-1P, 2-Methyl-4-[3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2H-pyrazol-3-ol 284033-13-2P, 4-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2-methyl-2H-pyrazol-3-ol 284033-14-3P, 4-[4-Fluoro-2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]-2-methyl-2H-pyrazol-3-ol 284033-15-4P, 1-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4-methyl-1,4-dihydrotetrazol-5-one 284033-16-5P, 1-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4-methyl-1,4-dihydrotetrazol-5-one 284033-17-6P, 1-Methyl-4-[3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1,4-dihydrotetrazol-5-one 284033-18-7P, 1-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-4-methyl-1,4-dihydrotetrazol-5-one 284033-20-1P, 1-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-[1,2,3]triazol-4-ol 284033-21-2P, 1-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-[1,2,3]triazol-4-ol 284033-22-3P, 1-[3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-[1,2,3]triazol-4-ol 284033-23-4P, 1-[5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-1H-[1,2,3]triazol-4-ol 284033-25-6P, 3-[4-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2H-isoxazol-5-one 284033-26-7P, 3-[3,4-Difluoro-2-(4-iodo-2-methylphenylamino)phenyl]-2H-

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 148553-50-8, Pregabalin 212631-61-3, PD 198306 **212631-79-3**, PD 184352 283602-39-1 284030-47-3, PD 254552 285125-85-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 142805-58-1, MEK kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 3438-16-2, 5-Chloro-2-methoxybenzoic acid 10308-82-4, Aminoguanidine nitrate 13194-68-8, 4-Iodo-2-methylaniline 212628-45-0, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 284033-40-5, (2,3-Difluoro-6-cyanophenyl)-(4-iodo-2-methylphenyl)amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of (2-heterocyclylphenyl)(4-iodophenyl)amines as MEK inhibitors for treatment of chronic pain)

RN 212631-79-3 HCAPLUS
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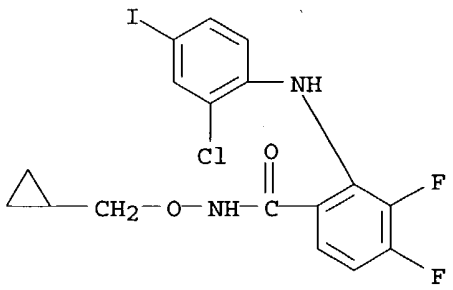

L112 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:63817 HCAPLUS
DN 134:131530
ED Entered STN: 26 Jan 2001
TI Preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for the treatment of chronic pain
IN Barrett, Stephen Douglas; Bridges, Alexander James; Tecle, Haile; Dixon, Alistair; Lee, Kevin; Pinnock, Robert Denham
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**
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	WO 2001005390	A3	20010517		
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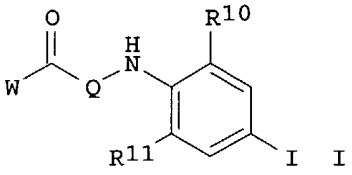

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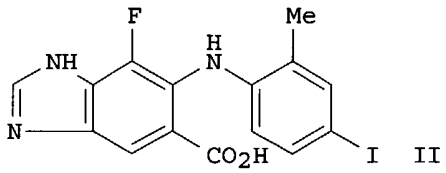


II

AB The title compds. (I) [wherein W = OR1, NR2OR1, NRARB, NR2NRARB, O(CH2)2-4NRARB, or NR2(CH2)2-4NRARB; R1 = H, (phenyl)alkyl,

(phenyl)alkenyl, (phenyl)alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkylalkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, or (CH2)2-4NRCRD; R2 = H, (cyclo)alkyl, Ph, heterocyclyl, or cycloalkylmethyl; RA = H, (cycloalkyl)alkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkynyl, cycloalkyl, Ph, heterocyclyl, heterocyclylalkyl, aminosulfonylphenyl(alkyl), aminosulfonyl(cyclo)alkyl, aminosulfonylcycloalkylalkyl, or (CH2)2-4NRCRD; RB, RC, and RD = independently H, (cyclo)alkyl, alkenyl, alkynyl, or Ph; or NRCRD = morpholinyl, piperizinyl, pyrrolidinyl, or piperidinyl; Q = a variety of (un)substituted benzo-fused heterocycles; R10 and R11 = independently H, Me, halo, or NO2] were prepared for the treatment of chronic pain. For example, cycloaddn. of Me 4,5-diamino-3-fluoro-2-(2-methylphenylamino)benzoate (5-step preparation given) with formic acid gave Me 7-fluoro-6-(2-methylphenylamino)-1H-benimidazole-5-carboxylate (87%). Iodination using benzyltrimethylammonium dichloroiodinate and ZnCl2 in AcOH (68%) and deesterification using potassium trimethylsilanolate in THF afforded PD 205293 (II) in 9% yield. II displayed an APK IC50 of 14 nM and an IC50 ≥ 10 μM against colon 26 cells. Biol. assays indicated that MEK inhibitors exert an antiallodynic effect in CCI-induced neuropathic rats when administered intrathecally and that the antiallodynic effect correlates with the affinity of the compds.

ST phenylamino benzimidazole prepn mek inhibitor; benzimidazole prepn analgesic; benzo fused heterocycle prepn chronic pain treatment

IT Pain
Skin, disease
(allodynia, treatment; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT Vitamins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(avitaminosis, treatment of pain associated with; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT Kidney, disease
(failure, treatment of pain associated with; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT Analgesics
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT Pain
(treatment of idiopathic and post-operative; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT Alcoholism
Arthritis
Hypothyroidism
Inflammation
(treatment of pain associated with; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT 74124-04-2P, Cyclopropylmethoxylamine hydrochloride 113211-15-7P, 2-Cyclopropylmethoxyisoindole-1,3-dione 197520-71-1P, 5-Nitro-2,3,4-trifluorobenzoic acid 284030-57-5P, 4-Amino-2,3-difluoro-5-nitrobenzoic acid 284030-58-6P, Methyl 4-amino-2,3-difluoro-5-nitrobenzoate 284030-59-7P, Methyl 4-amino-3-fluoro-2-(2-methylphenylamino)-5-nitrobenzoate 284030-60-0P, Methyl 4,5-diamino-3-fluoro-2-(2-methylphenylamino)benzoate 284030-61-1P, Methyl 7-fluoro-6-(2-methylphenylamino)-1H-benzimidazole-5-carboxylate 284030-62-2P, Methyl 7-fluoro-6-(4-iodo-2-methylphenylamino)-1H-benzimidazole-5-carboxylate 284030-63-3P, 2,3-Difluoro-4-hydroxy-5-nitrobenzoic acid 284030-64-4P, Methyl 2,3-difluoro-4-hydroxy-5-nitrobenzoate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(intermediate; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT 284486-99-3P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-1H-benzoimidazole-5-carboxylic acid pentafluorophenyl ester
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT 284030-28-0P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)benzoxazole-5-carboxylic acid 284030-29-1P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)benzothiazole-5-carboxylic acid 284030-30-4P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)benzo[1,2,5]thiadiazole-5-carboxylic acid 284030-31-5P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)benzo[1,2,5]oxadiazole-5-carboxylic acid 284030-32-6P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-2-(2-hydroxyethyl)-1H-benzimidazole-5-carboxylic acid 284030-33-7P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-2-(2-dimethylaminoethyl)-1H-benzimidazole-5-carboxylic acid 284030-34-8P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-1-acetylbenzimidazole-5-carboxylic acid 284030-35-9P, 8-Fluoro-7-(4-iodo-2-methylphenylamino)quinoxaline-6-carboxylic acid 284030-36-0P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-1H-benzotriazole-5-carboxylic acid 284030-47-3P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-1H-benzoimidazole-5-carboxylic acid cyclopropylmethoxyamide 284486-91-5P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-1H-benzoimidazole-5-carboxylic acid 321655-20-3P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-6,7-dihydro-1H-benzimidazole-5-carboxylic acid hydrochloride 321655-21-4P, 7-Fluoro-6-(4-iodo-2-methylphenylamino)-3H-benzimidazole-5-carboxylic acid (2-hydroxyethoxy)amide 321655-22-5P, 6-(2-Chloro-4-iodophenylamino)-7-fluoro-1H-benzimidazole-5-carboxylic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

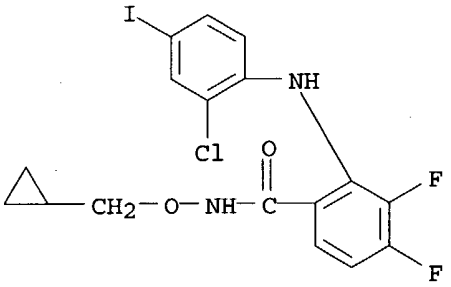
IT 148553-50-8, Pregabalin 212631-61-3, PD 198306 **212631-79-3**, PD 184352 283602-39-1 285125-85-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT 142805-58-1, MEK kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT 95-53-4, o-Toluidine, reactions 524-38-9, N-Hydroxyphthalimide 2516-33-8, Cyclopropanemethanol 61079-72-9, 2,3,4-Trifluorobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of phenylaminobenzimidazoles and analogs as MEK inhibitors for treatment of chronic pain)

RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)

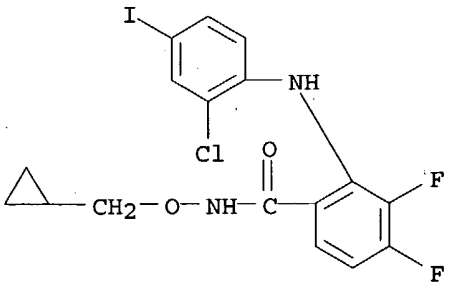


L112 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:805039 HCAPLUS
DN 133:344610
ED Entered STN: 15 Nov 2000
TI Specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells
IN Dent, Paul; Grant, Steven; Jarvis, W. David
PA Virginia Commonwealth University, USA
SO U.S., 19 pp.
CODEN: USXXAM
DT Patent
LA English
IC A01N043-02; A61K031-335
NCL 514449000
CC 1-6 (**Pharmacology**)
Section cross-reference(s): 7, 8
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6147107	A	20001114	US 1998-203342	19981220 <--
PRAI	US 1998-203342		19981220 <--		

AB Mammalian cancer cells are effectively killed when treated with a lethal agent (e.g. radiation or chemotherapeutic agents) in combination with an inhibitor specific for the p42/44 mitogen-activated protein (MAP) kinase cascade "proper". Inhibition of the p42/44 MAP kinase cascade with an agent such as PD184352 inhibits the ability of Raf protein kinases to phosphorylate and activate the enzymes MEK1 and MEK2. This in turn potentiates the apoptotic activity of radiation and the chemotherapeutic agents ara-C and taxol.
ST tumor sensitization MAP kinase cascade inhibition
IT Temperature effects, biological
(heat, sensitization to; specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT Radiosensitizers, biological
(pharmaceutical; specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT Light
(red, sensitization to high-intensity; specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT Electric field
IR radiation
Magnetic field
UV radiation
(sensitization to; specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT Antitumor agents
Light sensitization
(specific inhibition of the p42/44 mitogen-activated protein kinase

cascade sensitizes tumor cells)
IT Taxanes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT 137632-07-6, P44 MAP kinase 137632-08-7, P42 MAP kinase 139691-76-2, RAF kinase 142805-58-1 150316-14-6, MEK2 protein kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
IT 147-94-4, Ara-C 33069-62-4, Taxol 109511-58-2, U0126 167869-21-8, PD 98059 **212631-79-3**, PD 184352 305350-87-2, SL 327 305350-88-3, SW 073
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alessi; PD 098059 Is a Specific Inhibitor of the Activation of Mitogen-activated Portein Kinase Kinase in Vitro and in Vivo 1995, V270(46), P27489 HCAPLUS
(2) Anon; WO 9740842 1997 HCAPLUS
(3) Carter, S; Oncogene 1998, P15 HCAPLUS
(4) Dent, P; Leukemia 1998, P12
(5) Favata, M; The Journal of Biological Chemistry 1998, V273(29), P18623 HCAPLUS
(6) Jarvis; Molecular Pharmacology 1998, V54, P844 HCAPLUS
(7) Kavanaugh; Radiation Research 1998, V149, P579
(8) Wang; Leukemia 1999, V13, P1564 HCAPLUS
IT **212631-79-3**, PD 184352
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:771648 HCAPLUS
DN 134:67957
ED Entered STN: 03 Nov 2000
TI Specificity and mechanism of action of some commonly used protein kinase inhibitors
AU Davies, Stephen P.; Reddy, Helen; Caivano, Matilde; Cohen, Philip
CS Division of Signal Transduction Therapy, University of Dundee, Dundee, DD1 5EH, UK
SO Biochemical Journal (**2000**), 351(1), 95-105
CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): **1**

AB The specificities of 28 com. available compds. reported to be relatively selective inhibitors of particular serine/threonine-specific protein kinases have been examined against a large panel of protein kinases. The compds. KT 5720, Rottlerin and quercetin were found to inhibit many protein kinases, sometimes much more potently than their presumed targets, and conclusions drawn from their use in cell-based expts. are likely to be erroneous. Ro 318220 and related bisindoylmaleimides, as well as H89, HA1077 and Y 27632, were more selective inhibitors, but still inhibited two or more protein kinases with similar potency. LY 294002 was found to inhibit casein kinase-2 with similar potency to phosphoinositide (phosphatidylinositol) 3-kinase. The compds. with the most impressive selectivity profiles were KN62, PD 98059, U0126, PD 184352, rapamycin, wortmannin, SB 203580 and SB 202190. U0126 and PD 184352, like PD 98059, were found to block the mitogen-activated protein kinase (MAPK) cascade in cell-based assays by preventing the activation of MAPK kinase (MKK1), and not by inhibiting MKK1 activity directly. Apart from rapamycin and PD 184352, even the most selective inhibitors affected at least one addnl. protein kinase. Our results demonstrate that the specificities of protein kinase inhibitors cannot be assessed simply by studying their effect on kinases that are closely related in primary structure. The authors propose guidelines for the use of protein kinase inhibitors in cell-based assays.

ST protein kinase inhibitor mechanism specificity

IT 52660-18-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(2; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 9059-09-0
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3β,; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 141467-21-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(II; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 192230-91-4, MKK4 kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MKK3 and MKK4 and MKK7; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 90698-26-3, MAPKAP kinase 1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(isoform b; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 148640-14-6, Protein kinase B
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(isoform α; specificity and mechanism of action of commonly used protein kinase inhibitors)

IT 82-08-6, Rottlerin 117-39-5, Quercetin 2804-16-2, 10-[3-(1-Piperazinyl)propyl]-2-trifluoromethyl-phenothiazine 7439-93-2, Lithium, biological studies 7447-41-8, Lithium chloride, biological studies 19545-26-7, Wortmannin 34316-15-9, Chelerythrine 53123-88-9, Rapamycin 85753-43-1, K252c 103745-39-7, HA1077 108068-98-0, KT 5720

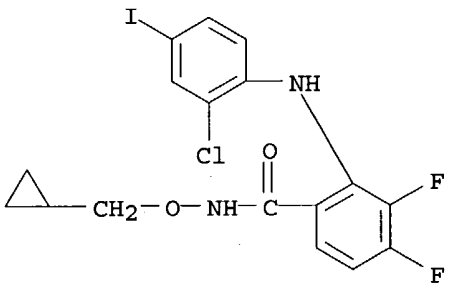
109511-58-2, U0126 112953-11-4, UCN1 125314-64-9, Ro 31-8220
127191-97-3, KN62 127243-85-0, H89 136194-77-9, Go6976 146986-50-7,
Y 27632 152121-30-7, SB 202190 152121-47-6, SB 203580 154447-36-6,
LY 294002 167869-21-8, PD 98059 **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(specificity and mechanism of action of commonly used protein kinase
inhibitors)
IT 9001-88-1, Phosphorylase kinase 9026-43-1, Protein kinase 51845-53-5,
Myosin light chain kinase 115926-52-8, Phosphoinositide 3-kinase
137632-08-7, ERK2 kinase 142008-29-5, CAMP-dependent protein kinase
142243-02-5, Mitogen-activated protein kinase 146838-30-4 154907-65-0,
Checkpoint kinase 156621-09-9, Mitogen-and stress-activated protein
kinase-1 165245-96-5, Stress-activated protein kinase 2a 172522-01-9,
AMP-activated protein kinase 176023-64-6, SAPK3 kinase 178037-70-2,
Serum/glucocorticoid-inducible protein kinase 179800-23-8,
Stress-activated protein kinase 2b 182938-08-5, Protein kinase ROCK-II
185156-08-5, Protein kinase C-related kinase-2 191808-15-8,
3-Phosphoinositide-dependent protein kinase 1 192333-55-4, SAPK4 kinase
194739-73-6, MKK6 kinase 197664-51-0, Lymphocyte-oriented protein kinase
212378-03-5, Protein kinase PRAK 244634-79-5, Kinase (phosphorylating),
gene chk2 protein
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(specificity and mechanism of action of commonly used protein kinase
inhibitors)
IT 141436-78-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(α, α and δ; specificity and mechanism of action of
commonly used protein kinase inhibitors)
IT 289898-51-7, JNK1 protein kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(α1; specificity and mechanism of action of commonly used protein
kinase inhibitors)
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alessi, D; FEBS Lett 1997, V402, P121 HCAPLUS
(2) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(3) Amano, M; J Biol Chem 1999, V274, P32418 HCAPLUS
(4) Asano, T; Cardiovasc Drug Rev 1998, V16, P76 HCAPLUS
(5) Badger, A; J Pharmacol Exp Ther 1996, V279, P1453 HCAPLUS
(6) Borsch-Haubold, A; J Biol Chem 1998, V273, P28766 HCAPLUS
(7) Brown, E; Nature 1995, V377, P441 HCAPLUS
(8) Caivano, M; J Immunol 2000, V164, P3018 HCAPLUS
(9) Carroll, M; Blood 1997, V90, P4947 HCAPLUS
(10) Cheng, K; Mol Cell Biochem 1983, V56, P183 HCAPLUS
(11) Cohen, P; Curr Opin Chem Biol 1999, V3, P459 HCAPLUS
(12) Cohen, P; Trends Cell Biol 1997, V7, P353 HCAPLUS
(13) Cuenda, A; FEBS Lett 1995, V364, P229 HCAPLUS
(14) Davis, P; FEBS Lett 1992, V259, P61
(15) DeSilva, D; J Immunol 1999, V160, P4175
(16) Deak, M; EMBO J 1998, V17, P4426 HCAPLUS
(17) Dudley, D; Proc Natl Acad Sci 1995, V92, P7686 HCAPLUS
(18) Eyers, P; Chem Biol 1998, V5, P321 HCAPLUS
(19) Eyers, P; FEBS Lett 1999, V451, P191 HCAPLUS
(20) Favata, M; J Biol Chem 1998, V273, P18623 HCAPLUS
(21) Fong, T; Cancer Res 1999, V59, P99 HCAPLUS
(22) Frantz, B; Biochemistry 1998, V37, P13846 HCAPLUS
(23) Graves, P; J Biol Chem 2000, V275, P5600 HCAPLUS
(24) Gschwendt, M; Biochem Biophys Res Commun 1994, V199, P93 HCAPLUS
(25) Gum, R; J Biol Chem 1998, V273, P15605 HCAPLUS

(26) Hall-Jackson, C; Chem Biol 1999, V6, P559 HCAPLUS
(27) Hall-Jackson, C; Oncogene 1999, V18, P2047 HCAPLUS
(28) Hers, I; FEBS Lett 1999, V460, P433 HCAPLUS
(29) Hidaka, H; Intracellular Signal Transduction, Advances in Pharmacology 1996, P193 HCAPLUS
(30) Itoh, K; Nat Med 1999, V5, P221 HCAPLUS
(31) Kamakura, S; J Biol Chem 1999, V274, P26563 HCAPLUS
(32) Kimura, K; Science 1996, V273, P245 HCAPLUS
(33) Lali, F; J Biol Chem 2000, V275, P7395 HCAPLUS
(34) Leopoldt, D; J Biol Chem 1998, V273, P7024 HCAPLUS
(35) Lingameneni, R; FEBS Lett 2000, V473, P265 HCAPLUS
(36) Mohammadi, M; EMBO J 1998, V17, P5896 HCAPLUS
(37) Moyer, J; Cancer Res 1997, V57, P4838 HCAPLUS
(38) Nakanishi, S; J Biol Chem 1992, V267, P2157 HCAPLUS
(39) Niggli, V; FEBS Lett 1999, V445, P69 HCAPLUS
(40) Picton, C; FEBS Lett 1992, V150, P191
(41) Sahai, E; Curr Biol 1999, V9, P136 HCAPLUS
(42) Sassone-Corsi, P; Science 1999, V285, P886 HCAPLUS
(43) Sebolt-Leopold, J; Nat Med 1999, V5, P810 HCAPLUS
(44) Shaw, M; Biochem J 1998, V336, P241 HCAPLUS
(45) Shawver, L; Clin Cancer Res 1997, V3, P1167 MEDLINE
(46) Stambolic, V; Curr Biol 1996, V6, P1664 HCAPLUS
(47) Sutherland, C; Biochem J 1993, V296, P15 HCAPLUS
(48) Tachibana, E; Acta Neurochir 1999, V141, P13 MEDLINE
(49) Thomas, G; Curr Opin Cell Biol 1997, V9, P782 HCAPLUS
(50) Thomson, S; EMBO J 1999, V18, P4779 HCAPLUS
(51) Tokumitsu, H; J Biol Chem 1990, V265, P4315 HCAPLUS
(52) Tong, L; Nat Struct Biol 1997, V4, P311 HCAPLUS
(53) Uehata, M; Nature 1997, V389, P990 HCAPLUS
(54) Wilson, K; Chem Biol 1997, V4, P423 HCAPLUS
(55) Woodburn, J; Cell Mol Biol Lett 1998, V3, P348
(56) Yu, L; J Biol Chem 1998, V273, P33455 HCAPLUS

IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(specificity and mechanism of action of commonly used protein kinase inhibitors)

RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:475534 HCAPLUS

DN 133:89333

ED Entered STN: 14 Jul 2000

TI Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors for use as antiviral agents

IN Bridges, Alexander James; Dudley, David Thomas; Gracheck, Stephen Joseph; Meyer, Annette Lynn; Saltiel, Alan Robert; Sebolt-Leopold, Judith

PA Warner-Lambert Company, USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-35
ICS A61K031-165; A61P031-12; A61P031-18; A61P031-22
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000040237	A1	20000713	WO 1999-US30484	19991221 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358438	AA	20000713	CA 1999-2358438	19991221 <--
EP 1140067	A1	20011010	EP 1999-966522	19991221 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
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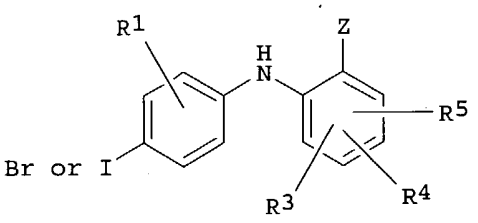
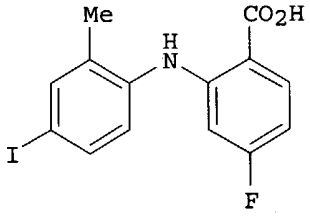
GI



I



II

AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid. For example, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. In assays evaluating the ability to prevent and inhibit growth of human cytomegalovirus (HCMV) and herpesvirus (HSV-1), 2-(2-methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-bromobenzamide (PD 177168) gave IC50 of 0.8 μM and 3.0 μM, resp., with TC50 of 9 μM and 11 μM, resp. PD 177168 also showed anti-HIV

activity with EC50 of 0.18 μM and TC50 of 5.95 μM. Thus, I are potent MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus.

ST diphenylamine std combinatorial prepn MEK inhibitor; bromophenylamino iodophenylamino benzamide prepn antiviral; benzamide prepn HIV hepatitis B herpes virus treatment

IT Hepatitis
(B, treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus)

IT Combinatorial library
Solid phase synthesis
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT Anti-AIDS agents
Antiviral agents
Human immunodeficiency virus 1
Toxicity
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus)

IT Cytomegalovirus
(treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus)

IT 282104-12-5, PD 178390
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(control compound; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 167869-21-8P, PD 098059 212630-41-6P, PD 170611 212630-94-9P, 5-Bromo-N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-57-7P, PD 185848 212631-61-3P, PD 198306 212631-67-9P, PD 184161 212631-78-2P, PD 203311 219778-04-8P, PD 185625 219778-52-6P, PD 180841
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 282103-63-3, PD 177098
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid

212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid
212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate
212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid
212628-52-9P 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid
212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid
212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid
212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid
212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid
212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-65-4P, 2,3,5-Trifluoro-4-(4-iodo-2-methylphenylamino)benzoic acid 212628-67-6P
212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-71-2P, 3-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P
212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid
212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid
212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-78-9P 212628-79-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212628-81-4P, N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-82-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide
212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)-benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide
212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-86-9P, [[5-Chloro-2-(4-iodo-2-methylphenylamino)benzoyl]amino]acetic acid 212628-87-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide 212628-88-1P, 5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide
212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P 212628-96-1P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P, [2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P, 5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P, 3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P, 4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-

methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-12-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide 212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide 212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P, 2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide 212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-56-6P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-60-2P, 5-Chloro-N-[3-(N,N-diethylamino)-2-hydroxypropyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-

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methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-42-7P, PD 171984 212630-43-8P, 2-(4-Bromo-2-methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-methylphenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P 212630-65-4P 212630-66-5P 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methyl-2-propyn-1-yloxy)benzamide 212630-68-7P 212630-69-8P 212630-70-1P 212630-71-2P 212630-72-3P 212630-73-4P 212630-74-5P 212630-75-6P 212630-76-7P 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide 212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-

N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-methylallyloxy)benzamide 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 212631-09-9P 212631-13-5P 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P 212631-29-3P 212631-33-9P 212631-35-1P 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P 212631-38-4P 212631-39-5P 212631-40-8P 212631-41-9P 212631-42-0P 212631-43-1P 212631-44-2P 212631-45-3P 212631-46-4P, PD 184386 212631-47-5P 212631-48-6P 212631-49-7P 212631-50-0P 212631-51-1P 212631-52-2P 212631-53-3P 212631-54-4P 212631-55-5P 212631-56-6P 212631-58-8P 212631-59-9P 212631-60-2P 212631-62-4P, PD 298127 212631-63-5P 212631-64-6P 212631-65-7P 212631-66-8P 212631-68-0P 212631-69-1P 212631-70-4P, PD 297189 212631-71-5P 212631-72-6P 212631-73-7P 212631-74-8P 212631-75-9P 212631-76-0P 212631-77-1P **212631-79-3P**, PD 184352 212631-80-6P 212631-81-7P 219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-60-3P, PD 188563 219794-13-5P 219794-21-5P, 2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester 277315-06-7P, (3-Hydroxypyrrolidin-1-yl)-[2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]methanone 277315-07-8P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-08-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-09-0P, [5-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-10-3P 277315-12-5P 277335-43-0P 278609-85-1P, PD 297190 278609-99-7P, PD 296711 278610-42-7P, PD 296770 278610-51-8P, PD 296767
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)-hydroxylamine 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 13194-68-8P, 2-Amino-5-iodotoluene 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde 212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P, 5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P 212631-85-1P, 5-Bromo-2,3 4-trifluorobenzoic acid 212631-86-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

IT 142805-58-1
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus)

IT 11028-71-0, Human herpesvirus 1
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors that are useful in the prevention and treatment of viral infections, especially HIV, hepatitis B, and herpesvirus)

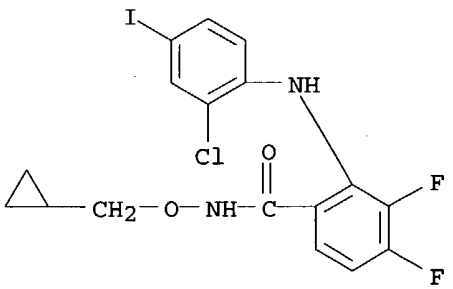
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Doherty, A; WO 9901421 A 1999 HCAPLUS
(2) Doherty, A; WO 9901426 A 1999 HCAPLUS
(3) Gibellini, D; JOURNAL OF IMMUNOLOGY 1998, V160(8), P3891 HCAPLUS
(4) Rodems, S; JOURNAL OF VIROLOGY 1998, V72(11), P9173 HCAPLUS
(5) Schang, L; JOURNAL OF VIROLOGY 1998, V72(7), P5626 HCAPLUS
(6) Shibutani, T; JOURNAL OF CLINICAL INVESTIGATION 1997, V100(8), P2054 HCAPLUS
(7) Univ New York; WO 9857175 A 1998 HCAPLUS

IT **212631-79-3P**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of acid)

RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:475533 HCAPLUS
DN 133:89332
ED Entered STN: 14 Jul 2000
TI Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors for the treatment of asthma
IN Bridges, Alexander James; Dudley, David Thomas; Mobley, James Leslie; Saltiel, Alan Robert
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM A61K031-195
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000040235	A2	20000713	WO 1999-US30419	19991221 <--
	WO 2000040235	A3	20001109		
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1140062	A2	20011010	EP 1999-968153	19991221 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9916785	A	20011023	BR 1999-16785	19991221 <--
	US 6696440	B1	20040224	US 2001-889091	20010711 <--
PRAI	US 1999-115086P	P	19990107 <--		
	WO 1999-US30419	W	19991221 <--		

OS MARPAT 133:89332
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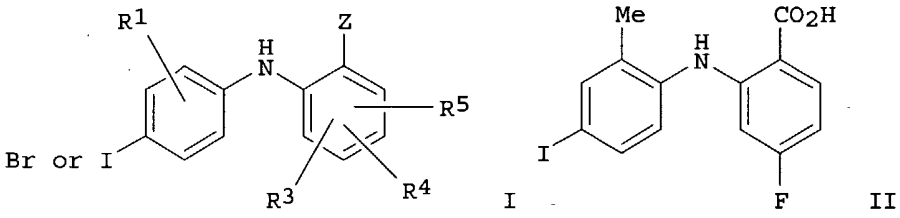


I II

AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid. For example, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. In an in vitro assay, 2-(2-methyl-4-iodophenylamino)-N-hydroxy-3,4-difluoro-5-bromobenzamide (PD 171984) prevented antigen-induced production of interleukin 5 (IL-5) by OVA-primed splenocytes with IC50 of 117 nM. In an adoptive-transfer assay using OVA-sensitized splenocytes cultured in the presence of PD 171984, the latter inhibited BAL eosinophilic lung inflammation by 99.82% at a dose of 10 μM in mice. PD 171984 also inhibited active OVA-induced eosinophilic lung inflammation in mice dosed orally at 100 μM for 4

days, suppressing BAL eosinophilia by 55.26%. Thus, I are potent MEK inhibitors that are useful in the prevention and treatment of asthma.

ST diphenylamine std combinatorial prepn MEK inhibitor; bromophenylamino iodophenylamino benzamide prepn antiasthmatic

IT Lung, disease
(eosinophilia, treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Combinatorial library
Solid phase synthesis
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Interleukin 5
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors for the prevention and treatment of asthma)

IT Antiasthmatics
(treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors for the prevention and treatment of asthma)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid
212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate
212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid
212628-52-9P 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid
212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid
212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid
212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid
212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid
212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-65-4P, 2,3,5-Trifluoro-4-(4-iodo-2-methylphenylamino)benzoic acid 212628-67-6P
212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-71-2P, 3-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P
212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid
212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid
212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-78-9P 212628-79-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212628-81-4P, N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-82-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide
212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)-

benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide 212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-86-9P, [[5-Chloro-2-(4-iodo-2-methylphenylamino)benzoyl]amino]acetic acid 212628-87-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide 212628-88-1P, 5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P 212628-96-1P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P, [2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P, 5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P, 3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P, 4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-12-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide 212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide 212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P, 2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide

212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-56-6P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-60-2P, 5-Chloro-N-[3-(N,N-diethylamino)-2-hydroxypropyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-68-0P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-69-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-71-5P, 5-Chloro-N-(3-diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-73-7P, 5-Chloro-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-75-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-77-1P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-piperidin-1-ylethyl)benzamide 212629-78-2P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperazin-1-ylethyl)benzamide 212629-79-3P, N-(2-Diethylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-80-6P, 5-Bromo-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-81-7P, N-(3-Hydroxypropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-82-8P, 5-Fluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-83-9P, N-(3-Diethylaminopropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-84-0P, N-(3-Diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-85-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-86-2P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(3-piperidin-1-ylpropyl)benzamide 212629-87-3P, 5-Bromo-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-88-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-89-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-90-8P, N-[3-(N,N-Diethylamino)-2-hydroxypropyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-91-9P 212629-92-0P 212629-93-1P, N-(2-Diisopropylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-94-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-95-3P,

5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-98-6P 212629-99-7P 212630-00-7P, N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-03-0P, 5-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212630-04-1P, N-Benzyloxy-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-05-2P, N-Benzyloxy-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-06-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(4-sulfamoylbenzyl)benzamide 212630-07-4P, N-(2-Hydroxyethyl)-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-08-5P, N-(2-Hydroxyethyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-09-6P, 2-(4-Iodo-2-methylphenylamino)-N-methyl-5-nitro-N-phenylbenzamide 212630-10-9P, 5-Chloro-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-11-0P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-12-1P, N-Allyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-13-2P, N-Benzyloxy-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-14-3P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-15-4P, N-Allyl-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212630-16-5P, N-Cyclopropyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-17-6P, 5-Bromo-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-18-7P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-19-8P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-20-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-21-2P, N-Allyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-22-3P, N-Allyl-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-23-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-24-5P, N-Cyclopropyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-25-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-26-7P, N-Benzyloxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-27-8P, N-Cyclohexyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-28-9P, N-Allyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-41-6P, PD 170611 212630-42-7P, PD 171984 212630-43-8P, 2-(4-Bromo-2-methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-methylphenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-

2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P 212630-65-4P 212630-66-5P 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methyl-2-propyn-1-yloxy)benzamide 212630-68-7P 212630-69-8P 212630-70-1P 212630-71-2P 212630-72-3P 212630-73-4P 212630-74-5P 212630-75-6P 212630-76-7P 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P
, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide
212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-91-6P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-94-9P, PD 177168 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-methylallyloxy)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide 212631-09-9P 212631-13-5P 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P 212631-29-3P 212631-33-9P 212631-35-1P 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P 212631-38-4P 212631-39-5P 212631-40-8P 212631-41-9P 212631-42-0P 212631-43-1P 212631-44-2P

212631-45-3P 212631-46-4P, PD 184386 212631-47-5P 212631-48-6P
212631-49-7P 212631-50-0P 212631-51-1P 212631-52-2P 212631-53-3P
212631-54-4P 212631-55-5P 212631-56-6P 212631-57-7P, PD 185848
212631-58-8P 212631-59-9P 212631-60-2P 212631-61-3P, PD 198306
212631-62-4P, PD 298127 212631-63-5P 212631-64-6P 212631-65-7P
212631-66-8P 212631-67-9P, PD 184161 212631-68-0P 212631-69-1P
212631-70-4P, PD 297189 212631-71-5P 212631-72-6P 212631-73-7P
212631-74-8P 212631-75-9P 212631-76-0P 212631-77-1P 212631-78-2P,
PD 203311 **212631-79-3P**, PD 184352 212631-80-6P 212631-81-7P
219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-60-3P, PD 188563 219778-04-8P, PD 185625 219778-52-6P, PD 180841 219794-13-5P 219794-21-5P,
2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester
277315-06-7P, (3-Hydroxypyrrolidin-1-yl)-[2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]methanone 277315-07-8P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone
277315-08-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-09-0P, [5-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone
277315-10-3P 277315-12-5P 277335-43-0P 278609-85-1P, PD 297190
278609-99-7P, PD 296711 278610-42-7P, PD 296770 278610-51-8P, PD 296767
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

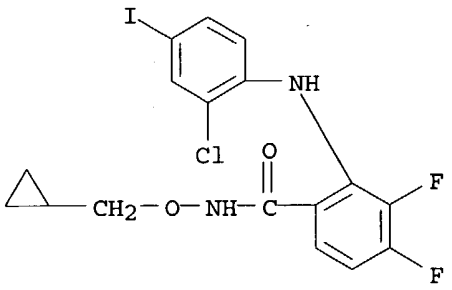
IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)-hydroxylamine 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 13194-68-8P, 2-Amino-5-iodotoluene 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde
212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P,
5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P 212631-85-1P,
5-Bromo-2,3 4-trifluorobenzoic acid 212631-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 142805-58-1
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors for the prevention and treatment of asthma)

IT **212631-79-3P**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:441667 HCAPLUS
DN 133:58616
ED Entered STN: 30 Jun 2000
TI Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors
IN Gowan, Richard Carleton; Sebolt-Leopold, Judith
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61P035-00
ICS A61K031-335; A61K031-35; A61K031-475; A61K031-335; A61K031-135; A61K031-475; A61K031-135; A61K031-335; A61K031-245; A61K031-475; A61K031-245; A61K031-335; A61K031-165; A61K031-475; A61K031-165; A61K031-35; A61K031-335; A61K031-475; A61K031-35
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037141	A1	20000629	WO 1999-US30485	19991221 <--
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1140291	A1	20011010	EP 1999-966523	19991221 <--
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	TR 200101871	T2	20011022	TR 2001-20010187119991221 <--	
	JP 2002532570	T2	20021002	JP 2000-589248	19991221 <--
	EE 200100339	A	20021015	EE 2001-339	19991221 <--
	ZA 2001004277	A	20020826	ZA 2001-4277	20010524 <--
	NO 2001003099	A	20010820	NO 2001-3099	20010621 <--
	HR 2001000473	A1	20020831	HR 2001-473	20010621 <--
	BG 105715	A	20020430	BG 2001-105715	20010718 <--
PRAI	US 1998-113291P	P	19981222 <--		
	US 1999-164788P	P	19991110 <--		
	WO 1999-US30485	W	19991221 <--		

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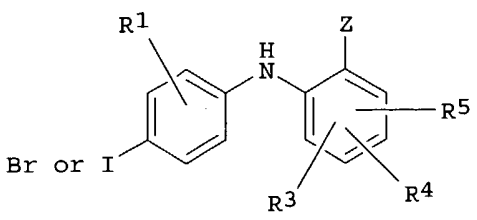

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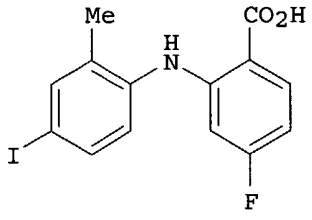


II

AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid. Thus, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. Combination chemotherapy of I with a known mitotic agent caused dramatic increases of apoptosis of colon and lung carcinoma cells. For instance, 2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide (PD 184352) in combination with paclitaxel resulted in 44% to 55% apoptosis, 6% to 18% increases over using either agent alone, of colon 26 carcinoma, HT-29 colon carcinoma, and A549 lung carcinoma cells.

ST diphenylamine std combinatorial prepn MEK inhibitor; bromophenylamino iodophenylamino benzamide prepn anticancer agent; benzamide bromophenylamino iodophenylamino prepn mitotic agent combination chemotherapy

IT Apoptosis
(increased efficacy in treatment of cancer with combination chemotherapeutics comprised of compns. of MEK inhibitors and known mitotic inhibitors)

IT Combinatorial library
Solid phase synthesis
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Antitumor agents
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors for use in combination with known mitotic inhibitors as anticancer agents)

IT 33069-62-4, Paclitaxel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased efficacy in treatment of cancer with combination chemotherapeutics comprised of compns. of MEK inhibitors and known mitotic inhibitors)

IT 57-22-7, Vincristine 865-21-4, Vinblastine 71486-22-1, Vinorelbine 114977-28-5, Docetaxel 162652-95-1, Vinflunine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased efficacy in treatment of cancer with combination chemotherapeutics comprised of compns. of MEK inhibitors and known mitotic inhibitors)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
212630-41-6P, 4-Fluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid
212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate
212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid
212628-52-9P 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid
212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid
212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid
212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid
212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid
212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-65-4P, 2,3,5-Trifluoro-4-(4-iodo-2-methylphenylamino)benzoic acid 212628-67-6P
212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-71-2P, 3-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P
212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid
212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid
212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-78-9P 212628-79-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212628-81-4P, N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-82-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide
212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)-benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide
212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-86-9P, [[5-Chloro-2-(4-iodo-2-methylphenylamino)benzoyl]amino]acetic acid 212628-87-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide 212628-88-1P, 5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide
212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P 212628-96-1P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P, [2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P, 5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-

iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P, 3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P, 4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-12-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide 212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide 212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P, 2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide 212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P,

5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-56-6P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-60-2P, 5-Chloro-N-[3-(N,N-diethylamino)-2-hydroxypropyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-68-0P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-69-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-71-5P, 5-Chloro-N-(3-diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-73-7P, 5-Chloro-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-75-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-77-1P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-piperidin-1-ylethyl)benzamide 212629-78-2P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperazin-1-ylethyl)benzamide 212629-79-3P, N-(2-Diethylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-80-6P, 5-Bromo-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-81-7P, N-(3-Hydroxypropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-82-8P, 5-Fluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-83-9P, N-(3-Diethylaminopropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-84-0P, N-(3-Diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-85-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-86-2P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(3-piperidin-1-ylpropyl)benzamide 212629-87-3P, 5-Bromo-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-88-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-89-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-90-8P, N-[3-(N,N-Diethylamino)-2-hydroxypropyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-91-9P 212629-92-0P 212629-93-1P, N-(2-Diisopropylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-94-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-95-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-98-6P 212629-99-7P 212630-00-7P, N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-03-0P, 5-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212630-04-1P, N-Benzyloxy-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-05-2P, N-Benzyloxy-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-06-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(4-sulfamoylbenzyl)benzamide 212630-07-4P, N-(2-Hydroxyethyl)-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-08-5P, N-(2-Hydroxyethyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-09-6P, 2-(4-Iodo-2-methylphenylamino)-N-methyl-5-nitro-N-phenylbenzamide 212630-10-9P, 5-Chloro-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-11-0P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-12-1P, N-Allyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-13-2P, N-Benzyloxy-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-14-3P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-15-4P, N-Allyl-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212630-16-5P, N-Cyclopropyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-17-6P, 5-Bromo-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-18-7P, 5-Chloro-2-(4-iodo-2-

methylphenylamino)-N-methyl-N-phenylbenzamide 212630-19-8P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-20-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-21-2P, N-Allyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-22-3P, N-Allyl-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-23-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-24-5P, N-Cyclopropyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-25-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-26-7P, N-Benzyloxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-27-8P, N-Cyclohexyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-28-9P, N-Allyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-42-7P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212630-43-8P, 2-(4-Bromo-2-methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-methylphenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P 212630-65-4P 212630-66-5P 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methyl-2-propyn-1-yloxy)benzamide 212630-68-7P 212630-69-8P 212630-70-1P 212630-71-2P 212630-72-3P 212630-73-4P 212630-74-5P 212630-75-6P 212630-76-7P 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P,

2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide 212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-91-6P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-94-9P 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-methylallyloxy)benzamide 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide 212631-09-9P 212631-13-5P 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P 212631-29-3P 212631-33-9P 212631-35-1P 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P 212631-38-4P 212631-39-5P 212631-40-8P 212631-41-9P 212631-42-0P 212631-43-1P 212631-44-2P 212631-45-3P 212631-46-4P 212631-47-5P 212631-48-6P 212631-49-7P 212631-50-0P 212631-51-1P 212631-52-2P 212631-53-3P 212631-54-4P 212631-55-5P 212631-56-6P 212631-57-7P 212631-58-8P 212631-59-9P 212631-60-2P 212631-61-3P 212631-62-4P 212631-63-5P 212631-64-6P 212631-65-7P 212631-66-8P 212631-67-9P 212631-68-0P 212631-69-1P 212631-71-5P 212631-72-6P 212631-73-7P 212631-74-8P 212631-75-9P 212631-76-0P 212631-77-1P 212631-78-2P **212631-79-3P** 212631-80-6P 212631-81-7P 219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-60-3P 219778-04-8P 219778-52-6P 219794-13-5P 219794-21-5P, 2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester 277315-06-7P, (3-Hydroxypyrrolidin-1-yl)-[2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]methanone 277315-07-8P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-08-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-09-0P, [5-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-10-3P 277315-12-5P 277335-43-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)-hydroxylamine 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 13194-68-8P, 2-Amino-5-iodotoluene 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde 212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P, 5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P 212631-85-1P, 5-Bromo-2,3 4-trifluorobenzoic acid 212631-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 142805-58-1
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors for use in combination with known mitotic inhibitors as anticancer agents)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

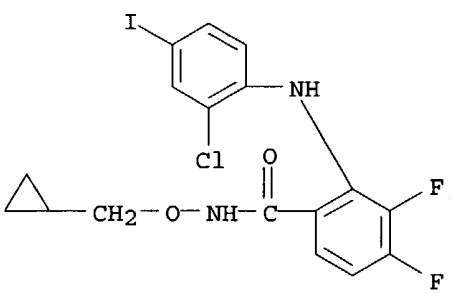
RE

(1) Ciba Geigy Ag; WO 9732604 A 1997 HCAPLUS
(2) Cowsert, L; US 5959097 A 1999 HCAPLUS
(3) de Souza; BRITISH JOURNAL OF CANCER 1997, V75(11), P1593 HCAPLUS
(4) Johnson, B; US 6002008 A 1999 HCAPLUS
(5) Lieu; CELL GROWTH & DIFFERENTIATION 1998, V9(9), P767 HCAPLUS
(6) Univ Texas; WO 9842830 A 1998 HCAPLUS
(7) Wang; BIOCHEMICAL PHARMACOLOGY 1998, V56(5), P635 HCAPLUS
(8) Warner Lambert Co; WO 9519970 A 1995 HCAPLUS
(9) Warner Lambert Co; WO 9837881 A 1998 HCAPLUS
(10) Wen-Ching, H; US 6040321 A 2000 HCAPLUS

IT **212631-79-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:420949 HCAPLUS
DN 133:73860
ED Entered STN: 23 Jun 2000
TI Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors
IN Dudley, David Thomas; Flory, Craig Mason; Saltiel, Alan Robert
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **1**, **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000035436	A2	20000622	WO 1999-US29783	19991215 <--
WO 2000035436	A3	20011018		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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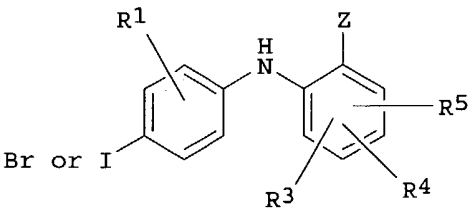
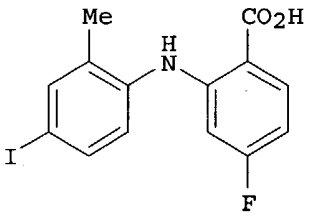
EP 1143957	A2	20011017	EP 1999-966278	19991215 <--
EP 1143957	A3	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1998-112544P	P	19981216 <--		
US 1999-164651P	P	19991110 <--		
WO 1999-US29783	W	19991215 <--		

OS MARPAT 133:73860
GI



I



II

AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic
acids to haloanilines and optional reduction or amidation of the acid. For

example, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. In assays against type II collagen induced arthritis in mice and monoarticular arthritis in rats, I showed potent anti-arthritic activity. I inhibited IL-1 induced stromelysin production in rabbit synovial fibroblast cell cultures with IC50 from 9 nM to 192 nM. Interleukin 1-alpha stimulated cartilage degradation was reduced by up to 75% in New Zealand white rabbits upon administration of I. Thus, I are potent MEK inhibitors useful in the prevention and treatment of rheumatoid arthritis or osteoarthritis.

ST diphenylamine std combinatorial prepn MEK inhibitor; bromophenylamino iodophenylamino benzamide prepn antiarthritic

IT Antiarthritics
Antirheumatic agents
Combinatorial library
Solid phase synthesis
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Interleukin 1
Interleukin 2
Proteoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate 212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid 212628-52-9P 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid 212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid 212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid 212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid 212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid 212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-65-4P, 2,3,5-Trifluoro-4-(4-iodo-2-methylphenylamino)benzoic acid 212628-67-6P 212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-71-2P, 3-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P 212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid 212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-

methylphenylamino)benzamide 212628-78-9P 212628-79-0P,
4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-80-3P,
4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212628-81-4P,
N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-82-5P,
4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide
212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)-
benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide
212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-
dimethylbenzamide 212628-86-9P, [[5-Chloro-2-(4-iodo-2-
methylphenylamino)benzoyl]amino]acetic acid 212628-87-0P,
4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide 212628-88-1P,
5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide
212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-
iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-
methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-
iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-
(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-
methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P 212628-96-1P,
[5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P,
[2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P,
[5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P,
5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-
methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-
difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P,
5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-
ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-
iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-
4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P,
3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-
pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-
iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P,
4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide
212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-
methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-
2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P,
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ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-
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3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-
ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-
(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-
(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-
methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide
212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-
ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-
N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-
2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P,
4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide
212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-
ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-
difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P,
5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-
ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-
methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P,
2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-
difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-
N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-
methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P,
2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-
ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-
difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-

methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide 212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-56-6P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-60-2P, 5-Chloro-N-[3-(N,N-diethylamino)-2-hydroxypropyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-68-0P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-69-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-71-5P, 5-Chloro-N-(3-diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-73-7P, 5-Chloro-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-75-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-77-1P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-piperidin-1-ylethyl)benzamide 212629-78-2P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperazin-1-ylethyl)benzamide 212629-79-3P, N-(2-Diethylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-80-6P, 5-Bromo-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-81-7P, N-(3-Hydroxypropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-82-8P, 5-Fluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-83-9P, N-(3-Diethylaminopropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-84-0P, N-(3-Diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-85-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-86-2P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(3-piperidin-1-ylpropyl)benzamide 212629-87-3P, 5-Bromo-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-88-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-89-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-

N-(3-piperidin-1-ylpropyl)benzamide 212629-90-8P, N-[3-(N,N-Diethylamino)-2-hydroxypropyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-91-9P 212629-92-0P 212629-93-1P, N-(2-Diisopropylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-94-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-95-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-98-6P 212629-99-7P 212630-00-7P, N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-03-0P, 5-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212630-04-1P, N-Benzyloxy-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-05-2P, N-Benzyloxy-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-06-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(4-sulfamoylbenzyl)benzamide 212630-07-4P, N-(2-Hydroxyethyl)-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-08-5P, N-(2-Hydroxyethyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-09-6P, 2-(4-Iodo-2-methylphenylamino)-N-methyl-5-nitro-N-phenylbenzamide 212630-10-9P, 5-Chloro-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-11-0P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-12-1P, N-Allyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-13-2P, N-Benzyloxy-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-14-3P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-15-4P, N-Allyl-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212630-16-5P, N-Cyclopropyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-17-6P, 5-Bromo-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-18-7P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-19-8P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-20-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-21-2P, N-Allyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-22-3P, N-Allyl-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-23-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-24-5P, N-Cyclopropyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-25-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-26-7P, N-Benzyloxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-27-8P, N-Cyclohexyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-28-9P, N-Allyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P, [4-Chloro-2-(1H-tetrazol-5-yl)phenyl]-(4-iodo-2-methylphenyl)amine 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-40-5P, [4-Nitro-2-(1H-tetrazol-5-yl)-phenyl]-(4-iodo-2-methylphenyl)amine 212630-41-6P, 2-(2-Methyl-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide 212630-42-7P, 5-Bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212630-43-8P, 2-(4-Bromo-2-methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-

methylphenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P 212630-65-4P 212630-66-5P 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methyl-2-propyn-1-yloxy)benzamide 212630-68-7P 212630-69-8P 212630-70-1P 212630-71-2P 212630-72-3P 212630-73-4P 212630-74-5P 212630-75-6P 212630-76-7P 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide 212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P

, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-91-6P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-94-9P 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-

methylallyloxy)benzamide 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide 212631-09-9P 212631-13-5P 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P 212631-29-3P 212631-30-6P 212631-32-8P 212631-33-9P 212631-34-0P 212631-35-1P 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P 212631-38-4P 212631-39-5P 212631-40-8P 212631-41-9P 212631-42-0P 212631-43-1P 212631-44-2P 212631-45-3P 212631-46-4P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-3,4-difluoro-N-hydroxybenzamide 212631-47-5P 212631-48-6P 212631-49-7P 212631-50-0P 212631-51-1P 212631-52-2P 212631-54-4P 212631-55-5P 212631-56-6P 212631-57-7P, 2-(2-Chloro-4-iodophenylamino)-4-fluoro-N-hydroxybenzamide 212631-58-8P 212631-59-9P 212631-60-2P 212631-61-3P, N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-62-4P 212631-63-5P 212631-64-6P 212631-65-7P 212631-66-8P 212631-67-9P, 5-Bromo-2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212631-68-0P 212631-69-1P 212631-70-4P 212631-71-5P 212631-72-6P 212631-73-7P 212631-75-9P 212631-76-0P 212631-77-1P 212631-78-2P, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide **212631-79-3P**, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212631-80-6P 212631-81-7P 219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-60-3P, 2-(2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluorobenzamide 219778-04-8P, 2-(2-Chloro-4-iodophenylamino)-N-cyclobutylmethoxy-3,4-difluorobenzamide 219778-52-6P 219794-13-5P 219794-21-5P, 2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester 277315-06-7P, (3-Hydroxypyrrolidin-1-yl)-[2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]methanone 277315-07-8P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-08-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-09-0P, [5-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-10-3P 277315-12-5P 277335-40-7P 277335-43-0P 278609-85-1P, 2-(4-Iodophenylamino)-N-cyclopropylmethoxy-5-chloro-3,4-difluorobenzamide 278609-99-7P, 2-(4-Iodophenylamino)-5-chloro-3,4-difluorobenzoic acid 278610-42-7P, 2-(2-Chloro-4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid 278610-51-8P, 5-Chloro-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 79955-99-0, Stromelysin 1 142805-58-1, MEK protein kinase

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)-hydroxylamine 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene

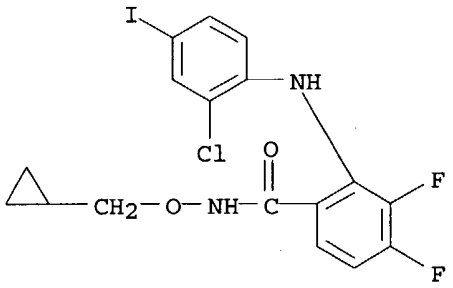
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 13194-68-8P, 2-Amino-5-iodotoluene 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde 212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P,

5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P 212631-85-1P, 5-Bromo-2,3 4-trifluorobenzoic acid 212631-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT **212631-79-3P**, 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



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DN 133:73859
ED Entered STN: 23 Jun 2000
TI Preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivatives as MEK inhibitors
IN Gilbertsen, Richard Buell
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
ICS A61K031-196; A61K031-166; A61K031-136; A61K031-41; A61K031-495; A61K031-4453; A61K031-40; A61K031-4465; A61K031-5375; A61K031-381; A61K031-341; A61K031-18; A61P037-06
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **1**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000035435	A1	20000622	WO 1999-US29591	19991214 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346684	AA	20000622	CA 1999-2346684	19991214 <--

EP 1140046 A1 20011010 EP 1999-966203 19991214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
TR 200101704 T2 20011121 TR 2001-20010170419991214 <--
JP 2002532414 T2 20021002 JP 2000-587756 19991214 <--
ZA 2001003765 A 20020509 ZA 2001-3765 20010509 <--
PRAI US 1998-112369P P 19981215 <--
WO 1999-US29591 W 19991214 <--
OS MARPAT 133:73859
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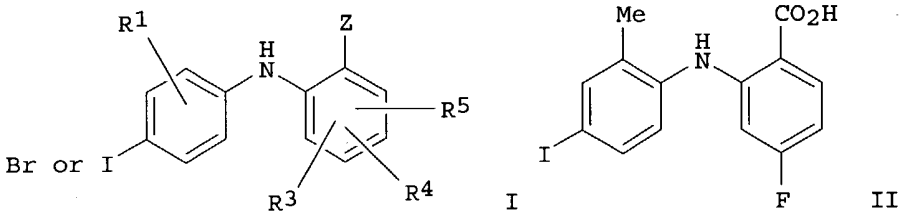


AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid. For example, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. In a mixed lymphocyte (or leukocyte) reaction (MLR) assay, 2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide (PD 184352) improved histocompatibility and gave IC50 of 186 nM. PD 184352 demonstrated potent immunosuppressive activity by causing almost total inhibition of Con A induced T cell proliferation at the highest dose tested (10.o μM) with IC50 of 340 nM. Thus, I are potent MEK inhibitors with immunosuppressive properties that are useful for preventing and controlling the rejection of transplants in mammals.

ST diphenylamine std combinatorial prepn MEK inhibitor; bromophenylamino iodophenylamino benzamide prepn immunosuppressant; benzamide bromophenylamino iodophenylamino prepn transplant rejection prevention treatment

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Combinatorial library
Immunosuppressants
Solid phase synthesis
Toxicity
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT CD28 (antigen)
CD3 (antigen)
Interleukin 2
Phytohemagglutinins
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT T cell (lymphocyte)
(proliferation; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT Interferons
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(γ; preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212630-42-7P, PD 171984 212630-94-9P, PD 177168 212631-46-4P, PD 184386 212631-57-7P, PD 185848 212631-61-3P, PD 198306 212631-67-9P, PD 184161 212631-78-2P, PD 203311 **212631-79-3P**, PD 184352
219778-04-8P, PD 185625 219778-52-6P, PD 180841
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-43-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-46-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-48-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212628-44-9P, 3,4,5-Trifluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-45-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-47-2P, 5-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid
212628-49-4P, Sodium 5-Chloro-2-(4-iodo-2-methylphenylamino)benzoate
212628-50-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-51-8P, 2-(2-Chloro-4-iodophenylamino)-5-nitrobenzoic acid
212628-52-9P 212628-53-0P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid 212628-54-1P, 2-(2-Fluoro-4-iodophenylamino)-5-nitrobenzoic acid
212628-55-2P, 2-(4-Bromo-2-methylphenylamino)-4-fluorobenzoic acid
212628-56-3P, 2-(2-Bromo-4-iodophenylamino)-5-nitrobenzoic acid
212628-57-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluorobenzoic acid
212628-58-5P, 3-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-59-6P, 3,4-Difluoro-2-(4-iodo-2-methoxyphenylamino)benzoic acid
212628-60-9P, 4-Chloro-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-61-0P, 2-(4-Iodo-2-methylphenylamino)benzoic acid 212628-62-1P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-63-2P, 5-Iodo-2-(4-iodo-2-methylphenylamino)benzoic acid 212628-65-4P, 2,3,5-Trifluoro-4-(4-iodo-2-methylphenylamino)benzoic acid 212628-67-6P
212628-69-8P, 2-(4-Iodophenylamino)-5-methoxybenzoic acid 212628-71-2P, 3-Chloro-2-(2-chloro-4-iodophenylamino)benzoic acid 212628-72-3P, 2-Fluoro-6-(4-iodo-2-methylphenylamino)benzoic acid 212628-73-4P
212628-74-5P, 5-Methyl-2-(4-iodo-2-methylphenylamino)benzoic acid
212628-75-6P, 2-Chloro-6-(4-iodo-2-methylphenylamino)benzoic acid

212628-76-7P, 2-(4-Iodo-2-methylphenylamino)-4-nitrobenzoic acid 212628-77-8P, 5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-78-9P 212628-79-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212628-81-4P, N-Ethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-82-5P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-83-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(1H-tetrazol-5-yl)-benzamide 212628-84-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)benzamide 212628-85-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-86-9P, [[5-Chloro-2-(4-iodo-2-methylphenylamino)benzoyl]amino]acetic acid 212628-87-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propylbenzamide 212628-88-1P, 5-Bromo-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212628-89-2P, N,N-Diethyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-90-5P, 4-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212628-91-6P, N,N-Diethyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212628-92-7P, N-Butyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212628-93-8P, 5-Chloro-N,N-diethyl-2-(4-iodo-2-methylphenylamino)benzamide 212628-94-9P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N,N-dimethylbenzamide 212628-95-0P 212628-96-1P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-97-2P, [2-(4-Iodo-2-methylphenylamino)-5-nitrophenyl]methanol 212628-98-3P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]methanol 212628-99-4P, 5-Bromo-3,4-difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-00-0P, N-(2,3-Dihydroxypropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-01-1P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-02-2P, 3,4-Difluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-03-3P, N-(2,3-Dihydroxypropyl)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-04-4P, 3,4-Difluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-05-5P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-06-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-07-7P, 4-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-08-8P, 5-Bromo-N-(3-dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-09-9P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-10-2P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-11-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-12-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-13-5P, N-(3-Dimethylaminopropyl)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-14-6P, N-Benzyl-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-15-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-hydroxyethyl)benzamide 212629-16-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-17-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-18-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-19-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-thiophen-2-ylethyl)benzamide 212629-20-4P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-21-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-morpholin-4-ylethyl)benzamide 212629-22-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-23-7P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-24-8P, 2-(4-Bromo-2-methylphenylamino)-N-(3-dimethylaminopropyl)-3,4-difluorobenzamide 212629-25-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-26-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyridin-4-ylethyl)benzamide 212629-27-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyridin-4-

ylethyl)benzamide 212629-28-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-hydroxypropyl)benzamide 212629-29-3P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-30-6P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenethylbenzamide 212629-31-7P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-thiophen-2-ylethyl)benzamide 212629-32-8P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-pyridin-4-ylmethylbenzamide 212629-33-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-phenethylbenzamide 212629-34-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-piperidin-1-ylethyl)benzamide 212629-35-1P, 5-Chloro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-36-2P, 5-Fluoro-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-37-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-pyridin-4-ylmethylbenzamide 212629-38-4P, 5-Bromo-N-[3-[4-(2-hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-39-5P, 5-Chloro-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-40-8P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-41-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-42-0P, 5-Bromo-N-(2-diethylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-43-1P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212629-44-2P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212629-45-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitrobenzoic acid phenethyl ester 212629-46-4P, N-[3-[4-(2-Hydroxyethyl)piperazin-1-yl]-propyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-47-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-pyridin-4-ylmethylbenzamide 212629-48-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-50-0P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-52-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-pyrrolidin-1-ylethyl)benzamide 212629-54-4P, 5-Chloro-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-56-6P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-58-8P, 5-Chloro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-60-2P, 5-Chloro-N-[3-(N,N-diethylamino)-2-hydroxypropyl]-2-(4-iodo-2-methylphenylamino)benzamide 212629-62-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-piperidin-1-ylethyl)benzamide 212629-64-6P, 5-Bromo-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-66-8P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-68-0P, N-[2-[Bis-(2-hydroxyethyl)amino]ethyl]-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-69-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-71-5P, 5-Chloro-N-(3-diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-73-7P, 5-Chloro-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-75-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-77-1P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(2-piperidin-1-ylethyl)benzamide 212629-78-2P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-piperazin-1-ylethyl)benzamide 212629-79-3P, N-(2-Diethylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-80-6P, 5-Bromo-N-(3-dimethylaminopropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-81-7P, N-(3-Hydroxypropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-82-8P, 5-Fluoro-N-(3-hydroxypropyl)-2-(4-iodo-2-methylphenylamino)benzamide 212629-83-9P, N-(3-Diethylaminopropyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-84-0P, N-(3-Diethylaminopropyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212629-85-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-86-2P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(3-piperidin-1-ylpropyl)benzamide 212629-87-3P, 5-Bromo-N-(2-diisopropylaminoethyl)-2-(4-iodo-2-methylphenylamino)benzamide

212629-88-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-morpholin-4-ylethyl)benzamide 212629-89-5P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-piperidin-1-ylpropyl)benzamide 212629-90-8P, N-[3-(N,N-Diethylamino)-2-hydroxypropyl]-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-91-9P 212629-92-0P 212629-93-1P, N-(2-Diisopropylaminoethyl)-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212629-94-2P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-95-3P, 5-Chloro-2-(4-iodo-2-methylphenylamino)thiobenzoic acid S-phenethyl ester 212629-98-6P 212629-99-7P 212630-00-7P, N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-03-0P, 5-Fluoro-N-(2-hydroxyethyl)-2-(4-iodo-2-methylphenylamino)benzamide 212630-04-1P, N-Benzyloxy-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-05-2P, N-Benzyloxy-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-06-3P, 2-(4-Iodo-2-methylphenylamino)-5-nitro-N-(4-sulfamoylbenzyl)benzamide 212630-07-4P, N-(2-Hydroxyethyl)-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-08-5P, N-(2-Hydroxyethyl)-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-09-6P, 2-(4-Iodo-2-methylphenylamino)-N-methyl-5-nitro-N-phenylbenzamide 212630-10-9P, 5-Chloro-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-11-0P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-12-1P, N-Allyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-13-2P, N-Benzyloxy-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-14-3P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-15-4P, N-Allyl-5-chloro-2-(4-iodo-2-methylphenylamino)benzamide 212630-16-5P, N-Cyclopropyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-17-6P, 5-Bromo-N-cyclopropyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-18-7P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-19-8P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-20-1P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(4-sulfamoylbenzyl)benzamide 212630-21-2P, N-Allyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-22-3P, N-Allyl-5-bromo-2-(4-iodo-2-methylphenylamino)benzamide 212630-23-4P, 5-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-24-5P, N-Cyclopropyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-25-6P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-26-7P, N-Benzyloxy-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-27-8P, N-Cyclohexyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-28-9P, N-Allyl-5-iodo-2-(4-iodo-2-methylphenylamino)benzamide 212630-29-0P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-30-3P, 2-(4-Iodo-2-methylphenylamino)-N-(3-methylbenzyl)-5-nitrobenzamide 212630-31-4P, 5-Iodo-2-(4-iodo-2-methylphenylamino)-N-methyl-N-phenylbenzamide 212630-32-5P, N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-33-6P, 5-Chloro-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-34-7P, 5-Bromo-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-35-8P, 5-Bromo-N-cyclohexyl-2-(4-iodo-2-methylphenylamino)benzamide 212630-36-9P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(3-methylbenzyl)benzamide 212630-37-0P, N-Cyclohexyl-2-(4-iodo-2-methylphenylamino)-5-nitrobenzamide 212630-38-1P 212630-39-2P, (4-Iodo-2-methylphenyl)-[2-(1H-tetrazol-5-yl)phenyl]amine 212630-41-6P, PD 170611 212630-43-8P, 2-(4-Bromo-2-methylphenylamino)-4-fluoro-N-hydroxybenzamide 212630-44-9P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)-N-methylbenzamide 212630-45-0P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-(terahydropyran-2-yloxy)benzamide 212630-46-1P, 5-Chloro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-47-2P, 4-Fluoro-N-hydroxy-2-(4-fluoro-2-methylphenylamino)benzamide 212630-48-3P, 4-Fluoro-N-hydroxy-2-(2-methylphenylamino)benzamide 212630-49-4P, 4-Fluoro-2-(4-fluoro-2-methylphenylamino)-N-(tetrahydropyran-2-yloxy)benzamide 212630-50-7P, 4-Fluoro-N-hydroxy-2-(4-chloro-2-

methylphenylamino)benzamide 212630-51-8P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-phenylmethoxybenzamide 212630-52-9P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-53-0P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-methoxybenzamide 212630-54-1P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-methoxybenzamide 212630-55-2P, 2-(4-Bromo-2-methylphenylamino)-N-ethoxy-3,4-difluorobenzamide 212630-56-3P, 5-Bromo-N-ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-57-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-58-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-isopropoxybenzamide 212630-59-6P, 4-Fluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-60-9P, 3,4-Difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-61-0P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(furan-3-ylmethoxy)benzamide 212630-62-1P, 5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methylphenylamino)benzamide 212630-63-2P, 5-Bromo-N-(but-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-64-3P 212630-65-4P 212630-66-5P 212630-67-6P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(1-methyl-2-propyn-1-yloxy)benzamide 212630-68-7P 212630-69-8P 212630-70-1P 212630-71-2P 212630-72-3P 212630-73-4P 212630-74-5P 212630-75-6P 212630-76-7P 212630-77-8P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-78-9P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(3-methyl-5-phenylpent-2-en-4-ynyloxy)benzamide 212630-79-0P, N-Ethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-80-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-81-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-82-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-propoxybenzamide 212630-83-6P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-propoxybenzamide 212630-84-7P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-85-8P, 5-Bromo-3,4-difluoro-2-(4-iodo-2-methylphenylamino)-N-isopropoxybenzamide 212630-86-9P, N-Cyclobutyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-87-0P, 2-(4-Bromo-2-methylphenylamino)-N-cyclobutyloxy-3,4-difluorobenzamide 212630-88-1P, N-Cyclopentyloxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-89-2P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopentyloxy-3,4-difluorobenzamide 212630-90-5P, N-Cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-91-6P, N-Cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide 212630-92-7P, 2-(4-Bromo-2-methylphenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide 212630-96-1P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-98-3P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-phenoxyethoxy)benzamide 212630-99-4P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-phenoxyethoxy)benzamide 212631-00-0P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-01-1P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(thiophen-2-ylmethoxy)benzamide 212631-02-2P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(thiophen-2-ylmethoxy)benzamide 212631-03-3P, 4-Fluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-04-4P, 3,4-Difluoro-2-(4-iodo-2-methylphenylamino)-N-(2-methylallyloxy)benzamide 212631-05-5P, 2-(4-Bromo-2-methylphenylamino)-3,4-difluoro-N-(2-methylallyloxy)benzamide 212631-06-6P, N-(But-2-enyloxy)-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-07-7P, N-(But-2-enyloxy)-3,4-difluoro-2-(4-iodo-2-methylphenylamino)benzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 212631-08-8P, 2-(4-Bromo-2-methylphenylamino)-N-(but-2-enyloxy)-3,4-difluorobenzamide 212631-09-9P 212631-13-5P 212631-15-7P, N-Cyclopentyloxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 212631-28-2P 212631-29-3P 212631-33-9P 212631-35-1P 212631-36-2P, 5-Chloro-N-hydroxy-2-(4-iodo-2-methylphenylamino)benzamide 212631-37-3P 212631-38-4P 212631-39-5P 212631-40-8P 212631-41-9P 212631-42-0P 212631-43-1P 212631-44-2P 212631-45-3P 212631-47-5P 212631-48-6P 212631-49-7P 212631-50-0P 212631-51-1P 212631-52-2P 212631-53-3P 212631-54-4P 212631-55-5P 212631-56-6P 212631-58-8P 212631-59-9P 212631-60-2P 212631-62-4P, PD 298127 212631-63-5P 212631-64-6P 212631-65-7P 212631-66-8P 212631-68-0P 212631-69-1P 212631-70-4P, PD 297189 212631-71-5P 212631-72-6P 212631-73-7P 212631-74-8P 212631-75-9P 212631-76-0P 212631-77-1P 212631-80-6P 212631-81-7P 219777-46-5P, N-(3-tert-Butylpropyn-2-yl)oxy-4-fluoro-2-(4-iodo-2-methylphenylamino)benzamide 219777-60-3P, PD 188563 219794-13-5P 219794-21-5P, 2-(4-Iodo-2-methylphenylamino)-5-nitrothiobenzoic acid S-benzyl ester 277315-06-7P, (3-Hydroxypyrrolidin-1-yl)-[2-(4-iodo-2-methylphenylamino)-5-nitrophenyl]methanone 277315-07-8P, [5-Bromo-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-08-9P, [5-Chloro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-09-0P, [5-Fluoro-2-(4-iodo-2-methylphenylamino)phenyl]-(3-hydroxypyrrolidin-1-yl)-methanone 277315-10-3P 277315-12-5P 277335-43-0P 278609-85-1P, PD 297190 278609-99-7P, PD 296711 278610-42-7P, PD 296770 278610-51-8P, PD 296767
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 11028-71-0, Concanavalin A 142805-58-1
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)-hydroxylamine 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

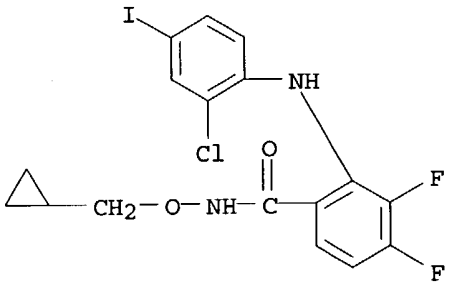
IT 13194-68-8P, 2-Amino-5-iodotoluene 57381-34-7P, 5-Chloro-2-fluorobenzonitrile 96515-79-6P, 5-Chloro-2-fluorobenzaldehyde 212631-82-8P, 5-Chloro-2-fluorobenzaldehyde oxime 212631-83-9P, 5-(5-Chloro-2-fluorophenyl)-1H-tetrazole 212631-84-0P 212631-85-1P, 5-Bromo-2,3 4-trifluorobenzoic acid 212631-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

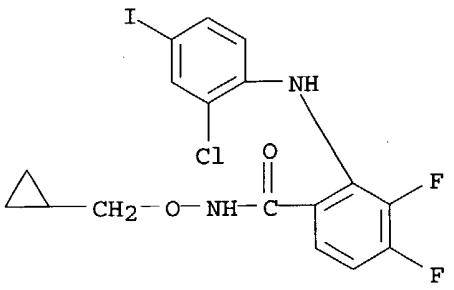
(1) Bridges, A; WO 9837881 A 1998 HCAPLUS
(2) Doherty, A; WO 9901421 A 1999 HCAPLUS
(3) Doherty, A; WO 9901426 A 1999 HCAPLUS
(4) Gen Hospital Corp; WO 9934792 A 1999 HCAPLUS
(5) Manna, S; JOURNAL OF IMMUNOLOGY 1999, V162(4), P2095 HCAPLUS
(6) Warner Lambert Co; EP 0316630 A 1989 HCAPLUS
(7) Warner Lambert Co; WO 9622985 A 1996 HCAPLUS

(8) Warner Lambert Co; WO 9631206 A 1996 HCAPLUS
(9) Williams, J; WO 9601111 A 1996 HCAPLUS
IT **212631-79-3P**, PD 184352
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(4-bromo or 4-iodo phenylamino)benzoic acid derivs. as MEK inhibitors by addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:444817 HCAPLUS
DN 131:208688
ED Entered STN: 21 Jul 1999
TI Blockade of the MAP kinase pathway suppresses growth of colon tumors in vivo
AU Sebolt-Leopold, Judith S.; Dudley, David T.; Herrera, Roman; Van Becelaere, Keri; Wiland, Amy; Gowan, Richard C.; Tecle, Haile; Barrett, Stephen D.; Bridges, Alexander; Przybranowski, Sally; Leopold, W. R.; Saltiel, Alan R.
CS Department of Cell Biology, Division of Warner-Lambert, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA
SO Nature Medicine (New York) (**1999**), 5(7), 810-816
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature America
DT Journal
LA English
CC 1-6 (**Pharmacology**)
AB The mitogen-activated protein kinase pathway is thought to be essential in cellular growth and differentiation. Here we report the discovery of PD 184352 (2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide), a highly potent and selective inhibitor of the upstream kinase MEK, that is orally active. Tumor growth was inhibited as much as 80% in mice with colon carcinomas of both mouse and human origin after treatment with this inhibitor. Efficacy was achieved with a wide range of doses with no signs of toxicity, and correlated with a reduction in the levels of activated mitogen-activated protein kinase in excised tumors. These data indicate that MEK inhibitors represent a promising, noncytotoxic approach to the clin. management of colon cancer.
ST MAP kinase blockade colon tumor inhibition; PD184352 MEK inhibitor colon tumor treatment
IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; blockade of MAP kinase pathway suppresses growth of colon tumors in vivo)

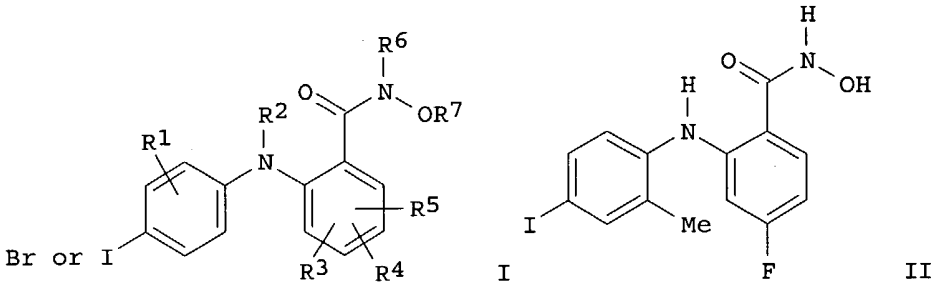
IT Antitumor agents
(colon; blockade of MAP kinase pathway suppresses growth of colon tumors in vivo)
IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blockade of MAP kinase pathway suppresses growth of colon tumors in vivo)
IT 142805-58-1, Protein kinase MEK
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; MEK inhibitors represent a promising, noncytotoxic approach to the clin. management of colon cancer)
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alessi, D; J Biol Chem 1995, V270, P27489 HCAPLUS
(2) Amundadottir, L; Oncogene 1998, V16, P737 HCAPLUS
(3) Anderson, N; Nature 1990, V343, P651 HCAPLUS
(4) Cobb, M; J Biol Chem 1995, V270, P14843 HCAPLUS
(5) Corbett, T; Cancer Res 1975, V35, P2434 HCAPLUS
(6) Cowley, S; Cell 1994, V77, P841 HCAPLUS
(7) Crews, C; Science 1992, V258, P478 HCAPLUS
(8) Dent, P; Science 1992, V257, P1404 HCAPLUS
(9) Dudley, D; Proc Natl Acad Sci USA 1995, V92, P7686 HCAPLUS
(10) Dudley, D; Signal Transduction Cell Cycle and Their Inhibitors
(11) Eliceiri, B; J Cell Biol 1998, V140, P1255 HCAPLUS
(12) Fiddes, R; Oncogene 1998, V16, P2803 HCAPLUS
(13) Her, J; Biochem J 1993, V296, P25 HCAPLUS
(14) Herrera, R; J Cell Science 1998, V111, P1039 HCAPLUS
(15) Hoshino, R; Oncogene 1999, V18, P813 HCAPLUS
(16) Khwaja, A; J Biol Chem 1998, V273, P18793 HCAPLUS
(17) Klemke, R; J Cell Biol 1997, V137, P481 HCAPLUS
(18) Lewis, T; Adv Cancer Res 1998, V74, P49 HCAPLUS
(19) Licato, L; Dig Dis Sci 1998, V43, P1454 HCAPLUS
(20) Licato, L; Gastroenterology 1997, V113, P1589 HCAPLUS
(21) Mandell, J; Amer J Pathol 1998, V153, P1411 HCAPLUS
(22) Mansour, S; Science 1994, V265, P966 HCAPLUS
(23) Marais, R; Cell 1993, V73, P381 HCAPLUS
(24) Milanini, J; J Biol Chem 1998, V273, P18165 HCAPLUS
(25) Pages, G; Proc Natl Acad Sci USA 1993, V90, P8319 HCAPLUS
(26) Pang, L; J Biol Chem 1995, V270, P13585 HCAPLUS
(27) Petit, A; Am J Pathol 1997, V151, P1523 HCAPLUS
(28) Potempa, S; Mol Biol Cell 1998, V9, P2185 HCAPLUS
(29) Ridley, A; Mol Cell Biol 1995, V15, P1110 HCAPLUS
(30) Seger, R; J Biol Chem 1992, V267, P14373 HCAPLUS
(31) Sivaraman, V; J Clin Invest 1997, V99, P1478 HCAPLUS
(32) Streit, M; J Mol Med 1996, V74, P253 HCAPLUS
(33) Takahashi-Tezuka, M; Mol Cell Biol 1998, V18, P4109 HCAPLUS
(34) Tanimura, S; Oncogene 1998, V17, P57 HCAPLUS
(35) Warne, P; Nature 1993, V364, P352 HCAPLUS
(36) Webb, C; Proc Natl Acad Sci USA 1998, V95, P8773 HCAPLUS
(37) Weidner, K; Nature 1996, V384, P173 HCAPLUS
IT **212631-79-3**, PD 184352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blockade of MAP kinase pathway suppresses growth of colon tumors in vivo)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:48698 HCAPLUS
DN 130:124900
ED Entered STN: 25 Jan 1999
TI Preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivatives as MEK inhibitors
IN Barrett, Stephen Douglas; Bridges, Alexander James; Doherty, Annette Marian; Dudley, David Thomas; Saltiel, Alan Robert; Tecle, Haile
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C259-10
ICS C07D295-08; C07D309-12; A61K031-165
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **1**, **63**
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9901426	A1	19990114		WO 1998-US13106	19980624	<--
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG						
	AU 9882627	A1	19990125		AU 1998-82627	19980624	<--
	AU 757046	B2	20030130				
	EP 993439	A1	20000419		EP 1998-932830	19980624	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
	BR 9810366	A	20000829		BR 1998-10366	19980624	<--
	NZ 501276	A	20001027		NZ 1998-501276	19980624	<--
	JP 2002511092	T2	20020409		JP 1999-507228	19980624	<--
	TW 396149	B	20000701		TW 1998-87110252	19980625	<--
	ZA 9805728	A	19990127		ZA 1998-5728	19980630	<--
	MX 9910649	A	20000430		MX 1999-10649	19991118	<--
	NO 9906491	A	19991229		NO 1999-6491	19991227	<--
	US 2003078428	A1	20030424		US 2002-163890	20020604	<--
PRAI	US 1997-51440P	P	19970701	<--			
	WO 1998-US13106	W	19980624	<--			
	US 2000-462239	B1	20000104	<--			

OS MARPAT 130:124900
GI



I II

AB The title compds. [I; R1 = H, OH, C1-8 alkyl, etc.; R2 = H; R3-R5 = H, OH, halo, etc.; R6 = H, C1-8 alkyl, aryl, etc.; R7 = H, C1-8 alkyl, C2-8 alkenyl, etc.], which are potent inhibitors of MEK and, as such, are effective in treating cancer and other proliferative diseases such as psoriasis, restenosis, autoimmune disease, or atherosclerosis, and also stroke, heart failure, hepatomegaly, cardiomegaly, diabetes, Alzheimer's disease, and cystic fibrosis, were prepared and formulated. Thus, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethylbenzene solution followed by addition of 2,4-difluorobenzoic acid in THF, and reaction of the resulting 4-fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid with O-(tetrahydro-2H-pyran-2-yl)hydroxylamine in the presence of diisopropylethylamine and PyBOP in THF/CH2Cl2, and treatment of the intermediate with ethanolic HCl afforded II which showed IC50 of 0.007 μM against MEK in vitro.

ST MEK inhibitor bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; antiproliferative bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; psoriasis bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; restenosis bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; autoimmune disease bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn; antiatherosclerotic bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; antitumor bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; stroke bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; heart failure bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn; hepatomegaly bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; antidiabetic bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation; Alzheimer's disease bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn; cystic fibrosis bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn; cardiomegaly bromophenylaminobenzhydroxamic iodophenylaminobenzhydroxamic acid prepn formulation

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)

IT Heart, disease
(failure, treatment of; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)

IT Liver, disease
(hepatomegaly, treatment of; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)

IT Antidiabetic agents
Antitumor agents
Cytotoxic agents
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)

IT Proliferation inhibition
(proliferation inhibitors; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT Artery, disease
(restenosis, treatment of; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT Brain, disease
(stroke, treatment of; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT Alzheimer's disease
Autoimmune disease
Cystic fibrosis
Psoriasis
(treatment of; preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT 212630-41-6P 212630-42-7P 212630-43-8P 212630-44-9P 212630-45-0P
212630-46-1P 212630-47-2P 212630-48-3P 212630-49-4P 212630-50-7P
212630-51-8P 212630-52-9P 212630-53-0P 212630-54-1P 212630-55-2P
212630-56-3P 212630-57-4P 212630-58-5P 212630-59-6P 212630-60-9P
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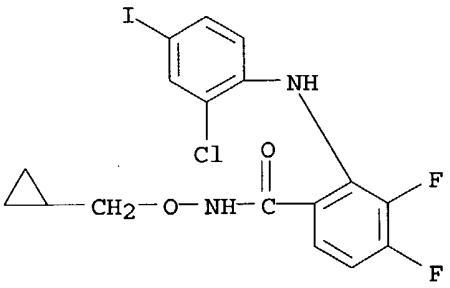
219778-43-5P 219778-48-0P 219778-52-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT 142805-58-1, Mek
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT 1583-58-0, 2,4-Difluorobenzoic acid 13194-68-8, 2-Amino-5-iodotoluene
176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
IT 212628-43-8P 212628-46-1P 212631-85-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as

MEK inhibitors)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bridges, A; US 5525625 A 1996 HCAPLUS
(2) Warner Lambert; WO 9837881 A 1998 HCAPLUS
IT **212631-79-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-bromo or 4-iodo phenylamino benzhydroxamic acid derivs. as MEK inhibitors)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



L112 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:603241 HCAPLUS
DN 129:230537
ED Entered STN: 23 Sep 1998
TI Preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock
IN Bridges, Alexander James
PA Warner Lambert Co., USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-195
ICS A61K031-165; A61K031-135; A61K031-41; A61K031-495; A61K031-445; A61K031-40; A61K031-44; A61K031-535; A61K031-38; A61K031-34; A61K031-18
CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9837881	A1	19980903	WO 1997-US23389	19971217	<--
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
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	ZA 9801578	A	19980902	ZA 1998-1578	19980225	<--
	US 6251943	B1	20010626	US 1999-355680	19990802	<--
PRAI	US 1997-39270P	P	19970228	<--		
	US 1997-56157P	P	19970819	<--		

WO 1997-US23389 W 19971217 <--
OS MARPAT 129:230537
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; R1 = H, OH, C1-8 alkyl, etc.; R2 = H; R3-R5 = H, OH, halo, etc.; Z = CO2R7, tetrazolyl, CONR6R7, etc.; R6, R7 = H, C1-8 alkyl, C2-8 alkenyl, etc.; R8 = H, C1-8 alkyl, aryl, etc.; R9 = H, C1-8 alkyl, C2-8 alkenyl, etc.], useful in treating or preventing septic shock, were prepared Thus, treatment of 2-amino-5-iodotoluene in THF with LDA/THF/heptane/ethenylbenzene followed by addition 2,4-difluorobenzoic acid afforded 47% III which showed IC50 of 0.019 μM against MEK in vitro.

ST MEK inhibitor phenylaminobenzoic acid phenylaminobenzamide prepn; septic shock phenylaminobenzoic acid phenylaminobenzamide prepn

IT Shock (circulatory collapse)
(septic; preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

IT 212628-48-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

IT 167869-21-8P 212628-43-8P 212628-44-9P 212628-45-0P 212628-46-1P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

IT 212631-00-0P 212631-01-1P 212631-02-2P 212631-03-3P 212631-04-4P
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212631-79-3P 212631-80-6P 212631-81-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

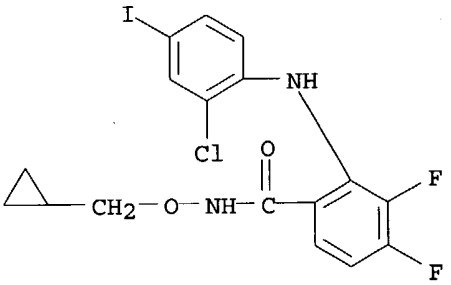
IT 146702-84-3, MEK kinase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

IT 352-33-0, 1-Chloro-4-fluorobenzene 1583-58-0, 2,4-Difluorobenzoic acid 6723-30-4 13194-68-8, 2-Amino-5-iodotoluene 176317-02-5, 1-Bromo-2,3,4-trifluorobenzene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

IT 57381-34-7P 96515-79-6P 212631-82-8P 212631-83-9P 212631-84-0P
212631-85-1P 212631-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bekemeier, H; AGENTS ACTIONS SUPPL 1982, P17 HCAPLUS
(2) Berner, N; JOURNAL OF MEDICINAL CHEMISTRY 1970, V13(3), P552 HCAPLUS
(3) Derijard, B; WO 9636642 A 1996 HCAPLUS
(4) Dudley, D; PROC NATL ACAD SCI 1995, V92(17), P7686 HCAPLUS
(5) Gaidukevich, A; KHIM-FARM ZH 1985, V19(3), P165 HCAPLUS
(6) Geppert, T; MOLECULAR MEDICINE 1994, V1(1), P93 HCAPLUS
(7) Ramanujam, P; PLANTA MEDICA 1974, V25(1), P43 HCAPLUS
(8) Shul'Ga, I; FARM ZH 1972, V27(3), P84 HCAPLUS

(9) Shul'Ga, T; FARM ZH 1988, V1, P42 HCAPLUS
(10) Signal Pharm Inc; WO 9722704 A 1997 HCAPLUS
(11) van der Bruggen, J; EUROPEAN JOURNAL OF CLINICAL INVESTIGATION 1997, V27(S1), PA19
(12) Warner Lambert Co; WO 9622985 A 1996 HCAPLUS
IT **212631-79-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-phenylaminobenzoic acids and its amides as MEK inhibitors for treating or preventing septic shock)
RN 212631-79-3 HCAPLUS
CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



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L113 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:171837 HCAPLUS
DN 136:232111
ED Entered STN: 08 Mar 2002
TI Process for making N-arylanthranilic acids and their derivatives
IN Chen, Michael Huai Gu; Davis, Edward Mark; Magano, Javier; Nanninga, Thomas Norman; Winkle, Derick Dale
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C227-08
ICS C07C231-12; C07C221-00; C07C253-30; C07C209-04; C07C231-02; C07C067-08
CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018319	A1	20020307	WO 2001-US22948	20010720 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001077044	A5	20020313	AU 2001-77044	20010720 <--
EP 1313694	A1	20030528	EP 2001-954824	20010720 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001013520	A	20030624	BR 2001-13520	20010720	<--
JP 2004507518	T2	20040311	JP 2002-523437	20010720	<--
US 2004039208	A1	20040226	US 2003-344294	20030207	
NO 2003000844	A	20030225	NO 2003-844	20030224	<--
PRAI US 2000-228206P	P	20000825	<--		
WO 2001-US22948	W	20010720			

OS CASREACT 136:232111; MARPAT 136:232111

AB N-arylanthranilic acids, their esters, amides, and hydroxamic esters are prepared by coupling 1 equivalent of an aniline derivative with 1 equivalent of an aromatic carboxylic acid carrying a leaving group, such as halo, alkyl- or arylsulfonyloxy, or phosphate, in presence of .apprx. 10 equivalent base. Thus, 2,3,4-F3C6H2CO2H was coupled with 2,4-Cl(I)C6H3NH2 in presence of LiN(CHMe2)2 in THF. The base was added at intervals at -20° with warming to room temp between addns. and the yield of 3,4-F2C6H3NHC6H3(I)Cl-4,2 was 78%. This compound was converted to the acid chloride and treated with cyclopropylmethoxyamine hydrochloride to give the N-cyclopropylmethoxyamide. The process is suitable for industrial production

ST arylanthranilic acid amide prepn manuf

IT Coupling reaction
(process for making N-arylanthranilic acids and their derivs.)

IT 212628-44-9P 219796-77-7P 303175-44-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for making N-arylanthranilic acids and their derivs.)

IT 644-62-2P 13625-57-5P 17626-44-7P, 2-Diphenylaminobenzoic acid 72990-98-8P 73323-82-7P 212628-46-1P 212631-61-3P 212631-78-2P **212631-79-3P** 313674-97-4P 313675-05-7P 391211-97-5P 402955-44-6P 402955-45-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for making N-arylanthranilic acids and their derivs.)

IT 60-29-7, Diethyl ether, uses 75-05-8, Acetonitrile, uses 77-76-9, 2,2-Dimethoxypropane 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses 629-14-1, 1,2-Diethoxyethane 1634-04-4, Methyl tert-butyl ether 7778-85-0, 1,2-Dimethoxypropane
RL: NUU (Other use, unclassified); USES (Uses)
(process for making N-arylanthranilic acids and their derivs.)

IT 100-61-8, N-Methylaniline, reactions 122-39-4, Diphenylamine, reactions 445-29-4, 2-Fluorobenzoic acid 496-15-1, Indoline 1201-31-6, 2,3,4,5-Tetrafluorobenzoic acid 1583-58-0, 2,4-Difluorobenzoic acid 13194-68-8, 4-Iodo-2-methylaniline 29632-74-4, 2-Fluoro-4-iodoaniline 42016-93-3, 2-Chloro-4-iodoaniline 61079-72-9, 2,3,4-Trifluorobenzoic acid 64063-37-2, 2,6-Dichloro-3-methylaniline 74124-04-2, Cyclopropylmethoxyamine hydrochloride 104799-67-9 104800-02-4 402955-41-3 402955-42-4 402955-43-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for making N-arylanthranilic acids and their derivs.)

IT 109-02-4, N-Methylmorpholine 141-52-6, Sodium ethoxide 530-62-1 865-47-4 1070-89-9, Sodium bis(trimethylsilyl)amide 2414-98-4, Magnesium ethoxide 4039-32-1, Lithium bis(trimethylsilyl)amide 4111-54-0, Lithium diisopropylamide 7580-67-8, Lithium hydride 7646-69-7, Sodium hydride 7693-26-7, Potassium hydride 7782-89-0, Lithium amide 7782-92-5, Sodium amide 7789-78-8, Calcium hydride 17242-52-3, Potassium amide 40949-94-8, Potassium bis(trimethylsilyl)amide 56602-33-6, BOP hexafluorophosphate
RL: RGT (Reagent); RACT (Reactant or reagent)
(process for making N-arylanthranilic acids and their derivs.)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

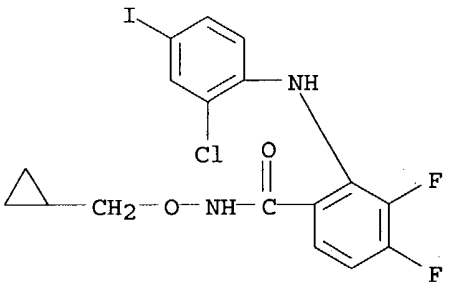
(1) Douglas, B; WO 0041994 A 2000 HCAPLUS

(2) James, B; WO 9837881 A 1998 HCAPLUS
(3) Marian, D; WO 9901421 A 1999 HCAPLUS
(4) Marian, D; WO 9901426 A 1999 HCAPLUS
(5) Parke Davis & Co; GB 935405 A 1963
(6) Warner Lambert Co; WO 0064856 A 2000 HCAPLUS

IT **212631-79-3P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for making N-arylanthranilic acids and their derivs.)

RN 212631-79-3 HCAPLUS

CN Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro- (9CI) (CA INDEX NAME)



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